Exhibit 2

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

CUYAHOGA COUNTY, OHIO, et al., Plaintiffs, v. PURDUE PHARMA LP, et al., Defendants.	)	Case No.: 1:17-OP-45004 JUDGE DAN AARON POLSTER
SUMMIT COUNTY, OHIO, et al., Plaintiffs, v. PURDUE PHARMA LP, et al., Defendants.	)	Case No. 1:18-OP-45090 JUDGE DAN AARON POLSTER

Expert Report of Henry Grabowski, PH.D.
May 10, 2019

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I. QUALIFICATIONS

1. My name is Henry G. Grabowski. I am a Professor Emeritus of Economics and the Director of the Program in Pharmaceuticals and Health Economics at Duke University. I received my Bachelor of Science degree in Engineering Physics from Lehigh University in 1962. In 1967, I obtained a doctorate in economics from Princeton University. After receiving my doctorate, I began my academic career at Yale University in 1967 and moved to Duke University in 1972 where I have been ever since.

2. I have studied the economics of the pharmaceutical industry over much of my career, and I have published numerous articles and books on this industry. Much of my research has focused on pharmaceutical competition and the economics of generic medications. I have written dozens of articles in this area. I have also conducted extensive research on pharmaceutical medication innovation. Under a series of grants from the National Science Foundation, I examined the economics of pharmaceutical research and development ("R&D") and the effect of various government policy actions on pharmaceutical medication development. The Congressional Budget Office has used my work in this regard to analyze the effects of the Drug Price Competition and Patent Term Restoration Act (commonly referred to as the Hatch-Waxman Act) on R&D returns and to analyze the proposed changes associated with the Health Security Act of 1993.

3. My teaching has also focused on the pharmaceutical industry, and includes creating and teaching a graduate course at Duke University on economics and policy issues in the pharmaceutical industry. I have testified several times before U.S. Congressional committees on pharmaceutical industry issues. For example, since 1994, I have testified on issues involving effective patent life and generic competition in pharmaceuticals, biosimilars, the Clinton Administration's health reform legislation, and the federal government's policy toward pediatric vaccines.

4. I have been an advisor and consultant to the National Academy of Sciences Institute of Medicine, Federal Trade Commission, General Accounting Office, and Office of Technology Assessment. I have also held visiting scholar appointments at the International Institute of Management in Berlin, Germany, the Health Care Financing Administration in Washington, D.C., the Office of Health Economics in London, England, and the Centre for Medicines Research in London, England. Until its acquisition by Gilead Sciences in 2003, I

served on the Board of Directors of Triangle Pharmaceuticals, Inc., a development-stage company that specialized in antiviral therapies.

5. A copy of my curriculum vitae is attached hereto as **Appendix 1**. It lists my publications that form the basis of my expertise, including all relevant publications over the last 10 years. **Appendix 2** provides a list of matters in which I have submitted an expert report or testified at trial or deposition over the last four years.

II. ASSIGNMENT

6. I have been retained by counsel for Endo Pharmaceuticals Inc. and Endo Health Solutions Inc. (together "Endo"), and Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc. (together "Par") to provide expert analysis, opinion, and testimony in response to the opinions, methods, and analyses described in the expert report of Dr. Meredith Rosenthal submitted on behalf of plaintiffs Cuyahoga and Summit Counties. Specifically, I have been asked to assess Dr. Rosenthal's description of pharmaceutical markets and the economics of pharmaceutical marketing activities, as well as her econometric analysis related to the relationship between pharmaceutical promotion and prescription sales.

7. I understand that this Cuyahoga County and Summit County litigation is brought against manufacturers, distributors, and pharmacies. I understand that Plaintiffs assert that "pharmaceutical manufacturers of prescription opioid drugs [engaged] in a massive false marketing campaign to drastically expand the market for such drugs and their own market share" and that "entities in the supply chain [realized] enormous financial rewards by refusing to monitor and restrict the improper distribution of those drugs."[1] Plaintiffs refer to "Purdue, Actavis, Cephalon, Janssen, Endo, Insys, and Mallinckrodt" as "Marketing Defendants."[2]

8. For this matter, I am being compensated at my standard billing rate of $800 per hour. I have been assisted in this matter by staff of Cornerstone Research, who worked under my direction. I receive compensation from Cornerstone Research based on its collected staff billings for its support of me in this matter. Neither my compensation in this matter nor my

[1] Complaint ¶¶ 1–2.

[2] Complaint ¶ 78. I refer to Marketing Defendants as Manufacturer Defendants in this report.

compensation from Cornerstone Research is in any way contingent or based on the content of my opinions or the outcome of this or any other matter.

9. In forming my opinions and conclusions, I have reviewed and considered the documents cited herein, such as documents produced in this litigation, as well as various public and private materials including documents and data pertinent to this matter. **Appendix 3** is a list of references considered in preparing my report. I have also relied on my years of academic and professional experience as an economist, including my experience in pharmaceutical economics. Although I have set forth citations to certain evidence supporting the analyses in this report, I may also rely upon any evidence from the materials that have been produced by the parties in this action, or that I consider relevant to the task assigned to me. All of the opinions stated in this report are stated to a reasonable degree of professional certainty. I reserve the right to supplement or amend my opinions in light of my ongoing review of the materials I have considered, as well as additional materials, including academic literature, data, documents, and depositions or other testimony that may subsequently come to light. Additionally, I reserve the right to comment on any opinions offered by plaintiffs' experts at deposition or trial. Finally, I reserve the right to use graphics or demonstratives at trial to illustrate the concepts discussed in my report.

III. SUMMARY OF OPINIONS

10. Dr. Rosenthal presents an incomplete and skewed view of the pharmaceutical industry (including the practice of educating physicians about products through promotional activities) and as a result, she overstates manufacturers' influence on prescribing. There are many participants in the pharmaceutical supply process through which prescription opioid medications are researched, developed, approved, manufactured, sold, distributed, prescribed, and ultimately made available to patients who have legitimate prescriptions. Manufacturers are just one part of the process. Other participants include wholesalers, pharmacists, physicians, health insurers, pharmacy benefit managers ("PBMs"), government regulatory bodies, public health agencies, and medical groups. Dr. Rosenthal fails to take this complexity into account, and therefore, Dr. Rosenthal's analyses are unreliable and cannot be used to show that allegedly improper promotion of prescription opioids led to "excess" opioid prescribing.

11. Dr. Rosenthal's conclusions rest entirely upon the unfounded assumption that "all or virtually all promotion by the manufacturer Defendants from 1995 to the present was unlawful."[3] Dr. Rosenthal's decision to rely upon "detailing contacts (i.e., the number of visits to physicians and other providers) to measure [all] promotion" and use shipment (aggregated by MMEs) data to purportedly measure prescription opioid sales are the additional building blocks for her conclusion that the Manufacturer Defendants' alleged unlawful promotion resulted in increased prescription opioid sales.[4] Dr. Rosenthal's unsupportable assumption, coupled with her decision to ignore everything else about the pharmaceutical industry, leads Dr. Rosenthal to draw the implausible conclusion that physicians were *perpetually and exponentially* swayed to prescribe more opioids by manufacturers' allegedly deceptive detailing messages. In other words, Dr. Rosenthal opines that the further in the past a detailing event occurred, the greater its impact in the future (*i.e.*, "negative depreciation"). Dr. Rosenthal's conclusion that a negative depreciation rate can be used in her model to explain the sales of prescription opioids is fundamentally flawed. There is no support for this proposition in the academic literature. In fact, all relevant literature runs contrary to this assertion.

12. Dr. Rosenthal's description of the impact of marketing activities in pharmaceutical markets is flawed and results in Dr. Rosenthal overstating the impact of pharmaceutical detailing on prescription opioid sales. Dr. Rosenthal fails to account for numerous other factors that are unrelated to marketing but impact physician prescribing decisions.

a. There are legitimate reasons why pharmaceutical manufacturers market their products, including to convey information about the availability and attributes (including both risks and benefits) of their products. Marketing, however, is just one of many factors physicians consider when making prescribing decisions. Other factors that affect physician prescribing decisions include characteristics of the available treatment options, characteristics of the patient, physician preferences and experience, regulatory requirements, and formulary placement. Among these factors, manufacturer marketing is consistently rated as less important than others for physicians in their prescribing decisions. Dr. Rosenthal ignores the impact of other factors on physician prescribing and

[3] Expert Report of Professor Meredith Rosenthal, dated March 25, 2019 ("Rosenthal Report"), ¶75.
[4] Rosenthal Report, ¶¶ 56, 11, 83.

incorrectly attributes all changes in physician prescribing behavior to manufacturers' detailing activities.

b. Dr. Rosenthal fails to adequately consider other sources of information relevant to prescription opioid medications. These additional sources of information include press coverage (which has been significant), clinical studies, medical journals, FDA approved labels (and associated label changes and black box warnings), and Center for Disease Control ("CDC") guidelines (and related changes to the guidelines).

c. Dr. Rosenthal also fails to address the impact that health insurers and PBMs have on physician prescribing behavior.

13. Dr. Rosenthal assumes that physician prescribing decisions were determined primarily by manufacturers' allegedly deceptive detailing messages, and that physicians were either unaware of or rejected the widely-available, public information concerning prescription opioids. This assumption is unfounded and implausible and renders her opinions unreliable.

14. Dr. Rosenthal's aggregate approach to estimation in effect assumes that all prescription opioid medications are the same. This assumption is unfounded and ignores that the prescription opioid market differs among medications, applications both in terms of active ingredients and in terms of uses, geography, physicians, and patients.

15. Dr. Rosenthal's methodology also relies on the incorrect assumption that all detailing visits are the same and equally impactful no matter who said what to whom about which product. Additionally, Dr. Rosenthal's model incorrectly assumes that all physician detailing has the same market expanding effect (i.e. resulting in additional opioid prescriptions that would not otherwise have been written). She ignores the market-share changing, competitive aspects of detailing, where one manufacturer attempts to gain sales by taking them from another manufacturer, in which prescriptions may shift from one product to another but the overall number of prescriptions does not necessarily increase. This effect is well detailed in academic literature. Because manufacturers may engage in detailing in part to take market share from competitors, physicians who already have a history of prescribing a particular medication are more likely to be targeted by detailers, a phenomenon that Dr. Rosenthal ignores.

16. Dr. Rosenthal's statistical framework suffers from additional flaws, which include conceptual mistakes and technical errors:

a. Dr. Rosenthal's modeling practices are fundamentally designed to achieve artificially good model fit and therefore cannot identify any causal relationship between prescription opioid shipments and detailing.

b. There is no variable in Dr. Rosenthal's model that identifies which detailing messages were purportedly deceptive, whether a physician who was detailed actually ever prescribed an opioid, let alone whether a physician who had been detailed actually wrote an opioid prescription that would not otherwise have been written or that was not medically appropriate. As such, Dr. Rosenthal's claim that her model can be easily adjusted later to separate any appropriate detailing from inappropriate detailing is not credible.

c. Dr. Rosenthal's use of multiple structural breaks in her estimation is nonsensical and unsupported. She does not cite any source or otherwise offer any justification as to why one would expect institutional changes taking place in August 2010 (such as changes in product formulations or the policy/regulatory environment) would manifest as a change to the impact of detailing instead of a change to the market itself.

d. Dr. Rosenthal's model suffers from significant omitted variable bias, i.e., she has not considered if other variables, such as economic and demographic controls that might explain trends in prescription opioid shipments better than manufacturers' detailing.

17. Even if Dr. Rosenthal's overall approach were an appropriate method of attempting to determine "excess" prescribing (which it is not), her methodology would still be flawed, and correcting even some of those flaws substantially impacts Dr. Rosenthal's results. For example, approximately 40 percent of Dr. Rosenthal's estimated "excess" prescribing is, in her model, attributable to detailing to oncologists, surgeons, and anesthesiologists that primarily prescribe opioids for uses that Dr. Rosenthal considers to be justified. Additionally, Dr. Rosenthal's estimates of "excess" prescribing is further reduced, and in some instances reduced to zero, when I control for total deflated healthcare expenditures and apply depreciation rates consistent with the realities of the marketplace and academic literature. This is further evidence that Dr. Rosenthal's analysis is unreliable and overstates the impact of the alleged deceptive practices.

18. Dr. Rosenthal's analysis cannot establish a causal link between Endo's detailing (a proxy she uses for all Endo promotion) of its prescription opioids and the volume of Endo's

opioid prescriptions (or opioid prescriptions in general). Additionally, Dr. Rosenthal has identified zero detailing conducted by Par. Indeed, Par did not conduct any detailing for its prescription opioid medications as supported by Dr. Rosenthal's own analysis of data. Thus, Dr. Rosenthal's model cannot in any event reliably be used to show that detailing by Par (there was none) had any impact on prescribing, let alone measure such impact.

IV. PHARMACEUTICAL SALES ARE INFLUENCED BY MANY PARTICIPANTS

19. To put Dr. Rosenthal's opinions in context, it is important to provide some background regarding the nature of the pharmaceutical industry and its complexities. The pharmaceutical supply process, through which patients with legitimate prescriptions are able to obtain prescription pharmaceuticals, is comprised of many different levels and participants, including not only manufacturers but also wholesalers, pharmacists, and physicians, as well as insurers, PBMs, government regulatory and public health agencies, and medical groups. Dr. Rosenthal's description of the pharmaceutical industry both fails to convey its complexity and ignores the impact that non-manufacturers have on prescription rates.

20. Pharmaceutical manufacturers fulfill the key role of developing the medications that treat medical conditions and enhance quality of life. Before pharmaceutical medications can be sold to patients, they must generally be approved by the FDA, which assesses whether the benefits of a medication outweigh its known and potential risks.[5] Many proposed medications are not approved.[6] Once approved, pharmaceutical medications can be prescribed by physicians to patients. While the FDA approves prescription medications, monitors their safety and efficacy, and approves manufacturers' marketing materials and labels associated with the prescription medications, the DEA plays a role in monitoring sales and distributions, especially for controlled substances. Before reaching a patient, pharmaceutical products are generally sold to wholesalers, stocked at pharmacies, processed

[5] "Development & Approval Process (Drugs)," FDA, https://www.fda.gov/drugs/development-approval-process-drugs, last accessed May 2019.

[6] "Is It True FDA is Approving Fewer Drugs Lately?" FDA, https://www.fda.gov/media/80203/download, last accessed May 2019.

through utilization and quality screening by PBMs, prescribed by licensed physicians, and dispensed at pharmacies by trained and licensed pharmacists.[7]

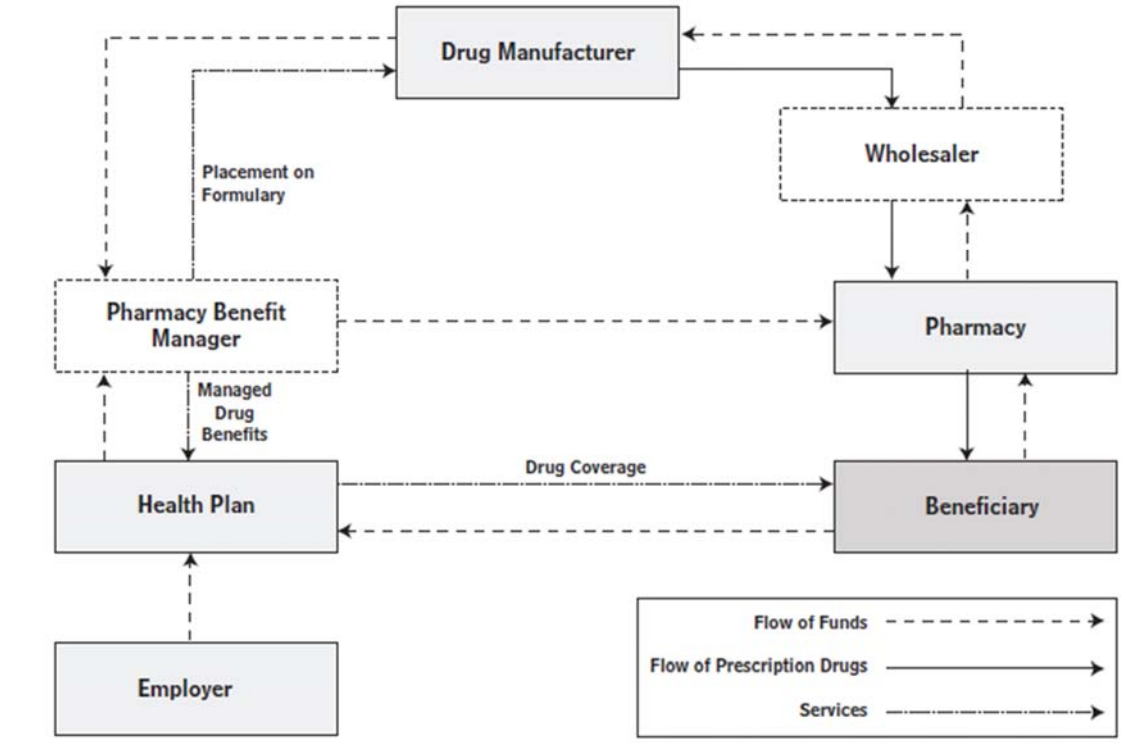
21. Prescription opioid medications, like other pharmaceutical medications, reach the patients through this complex pharmaceutical supply process with multiple participants. However, Dr. Rosenthal presents a transparently incomplete and skewed view of this complex process, omitting many of these participants from her discussion or downplaying their role. For example, Dr. Rosenthal understates the role that physicians play in prescribing prescription opioid medications and the role that wholesalers have in distributing them. She also fails to address the impact that health insurers and PBMs have on prescribing behavior. Dr. Rosenthal also diminishes the regulatory role of the FDA and ignores the oversight and enforcement roles of the DEA in pharmaceutical manufacturing, distribution, and marketing of prescription opioid medications.

22. Figure 1, based on a report from the Congressional Budget Office, depicts a stylized version of the pharmaceutical supply chain.[8] In the sections below, I provide an overview of the roles of each participant in the supply process, and how Dr. Rosenthal's narrow, incomplete view overstates the effect of manufacturer conduct on prescribing rates.

[7] "Follow The Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain," The Health Strategies Consultancy LLC, March 2005, ("The Health Strategies Consulting LLC (2005)") p. 1; "Prescription Drug Pricing in the Private Sector," Congressional Budget Office, 2007 ("Congressional Budget Office (2007)"), pp. 1, 10.

[8] Congressional Budget Office (2007) Figure 4, p. 11.

Figure 1. Flow of Funds for Single-Source Brand-Name Prescription Medications Purchased at a Retail Pharmacy and Managed by a Pharmacy Benefit Manager for an Employer's Health Plan



Source: Congressional Budget Office.

A. Pharmaceutical manufacturers

23. Pharmaceutical manufacturers develop, manufacture, and/or supply prescription medications. Within the pharmaceutical manufacturing industry, there are two business models: manufacturers of brand-name medications and manufacturers of generic medications.[9] Some pharmaceutical companies compete in both the branded and the generic parts of the industry. Endo sells primarily branded medication; while Par sells primarily generic medications.[10]

[9] The Health Strategies Consulting LLC (2005), p. 4.

[10] Endo Form 10-K, period ending December 31, 2017, p. 1; Par Form 10-K, period ending December 31, 2014, pp. 2–3; Endo Form 10-K, period ending December 31, 2007, p. 2. Par also owns Par Specialty Pharmaceuticals, which markets two branded products: Nascobal, a vitabmin B12 nasal spray, and Megace, a treatment for anorexia, cachexia, and unexplained weight loss associated with a diagnosis of AIDS. *See* Par Form 10-K, period ending December 31, 2014, pp. 2–3, 7.

24. Branded manufacturers devote significant resources to scientific R&D. Along the way, the manufacturer can apply for patent(s) for exclusivity, which can govern a medication itself, the way the medication is made, the way the medication is to be used, or the method of delivering and releasing the medication into the bloodstream; thus, companies often own multiple patents per medication.

25. Once approved for human use, branded manufacturers spend additional resources to disseminate information to increase physician awareness about their pharmaceutical products.[11] This is because a patient must have a prescription from a licensed physician or other appropriate healthcare professional in order to obtain a prescription medication from a pharmacist.[12] Branded manufacturers use information such as the clinical studies demonstrating the value of their pharmaceutical treatments as a way to help inform physicians about the attributes of their medications. In doing so, manufacturers sometimes attempt to differentiate their product from alternative products along a number of dimensions such as approved indications, treatment frequency or duration, and potential side effects.[13]

26. Generic manufacturers, meanwhile, generally do not develop new therapies. Rather, they typically enter a market after a brand product is no longer under patent protection or after challenging the validity of the patent, and compete by manufacturing therapeutically equivalent medications.[14] A generic medication is defined by the FDA as "a medication created to be the same as an existing approved brand-name medication in dosage form, safety, strength, route of administration, quality, and performance characteristics."[15] All states in the U.S. have laws addressing generic substitution, i.e., allowing or even mandating (except in limited circumstances) that pharmacists dispense cheaper generic versions of a branded medication, if generic version is available when filling a prescription written for a

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[11] "Step 5: FDA Post-Market Drug Safety Monitoring: Drug Advertising," FDA, https://www.fda.gov/patients/drug-development-process/step-5-fda-post-market-drug-safety-monitoring, last accessed May 2019; "Frequently Asked Questions about the FDA Drug Approval Process," FDA, https://www.fda.gov/drugs/special-features/frequently-asked-questions-about-fda-drug-approval-process, last accessed May 2019.

[12] "Pharmacist's Manual: Section IX–XIV," Diversion Control Division, DEA, U.S. Department of Justice, https://www.deadiversion.usdoj.gov/pubs/manuals/pharm2/pharm_content.htm, last accessed May 2019.

[13] "Beyond the Storm: Launch Excellence in the New Normal," *Insights into Pharmaceuticals and Medical Products*, McKinsey and Company, 2013, p. 5.

[14] Eickelberg, H. (2015), "The Prescription Drug Supply Chain 'Black Box,'" American Health Policy Institute ("Eickelberg (2015)"), p. 6.

[15] "Generic Drug Facts," FDA, June 1, 2018, https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm167991.htm, last accessed May 2019.

branded medication.[16] Generic manufacturers do not typically market to physicians or build awareness around their products or product attributes.

27. Once a pharmaceutical medication (whether branded or generic) is manufactured, it is generally shipped from the manufacturing site to wholesalers who then distribute the medication through the supply chain to pharmacies, physicians, hospitals, and/or PBMs. In some instances, pharmaceutical manufacturers may sell directly to other entities including retail pharmacy chains (such as CVS or Walgreens), hospitals, and government entities such as the Veterans Administration, but the majority of sales are to wholesalers.[17]

B. Wholesalers, pharmacies and physicians

28. Wholesalers, the largest of which are McKesson Corporation, Cardinal Health Inc., and AmerisourceBergen Corporation, purchase pharmaceutical products directly from manufacturers and then distribute them to a variety of customers.[18] In 2016, 95.7 percent of all U.S. pharmaceutical sales were made through distributors.[19] Wholesalers distribute pharmaceutical products to retail pharmacies, hospitals, long-term care facilities, and other agencies.[20] Wholesalers provide the link between pharmacies and manufacturers by warehousing pharmaceutical products and providing specialized services, such as specialty medication distribution, pharmaceutical repackaging, reimbursement support (e.g. processing "chargebacks" from pharmacy to manufacturer), and electronic order services.[21] Wholesalers have developed controlled substance monitoring programs "designed to detect and prevent opioid diversion."[22]

29. Before pharmaceutical products are dispensed to a patient, physicians must diagnose the patient's medical condition and prescribe the appropriate therapy or treatment for that

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[16] Grabowski, H. and Vernon, J. (1986), "Longer Patents for Lower Imitation Barriers: The 1984 Drug Act," *The American Economic Review*, 76(2), pp. 195–198, p. 196.

[17] The Health Strategies Consulting LLC (2005), p. 4.

[18] Fein, J., "2018 MDM Market Leaders | Top Pharmaceutical Distributors," *MDM*.

[19] "10 Pharmaceutical Distribution Trends to Know," *McKesson*, February 5, 2018, https://www.mckesson.com/blog/10-pharmaceutical-distribution-trends-to-know/, last accessed May 2019.

[20] Eickelberg (2015), p. 6.

[21] The Health Strategies Consulting LLC (2005), pp. 9, 19.

[22] "McKesson's Controlled Substance Monitoring Program," McKesson, https://www.mckesson.com/about-mckesson/fighting-opioid-abuse/controlled-substance-monitoring-program/, last accessed May 2019; "Fighting the Opioid Epidemic," AmerisourceBergen, https://www.amerisourcebergen.com/abcnew/fighting-the-opioid-epidemic, last accessed May 2019; "Cardinal Health Opioid Action Program", Cardinal Health, https://www.cardinalhealth.com/en/about-us/corporate-citizenship/opioid-action-program.html, last accessed May 2019.

condition.[23] When prescribing pharmaceutical treatments, the physician is responsible for ensuring the appropriate duration and dosage of the prescribed medication at inception, throughout treatment, and at discontinuation.

30. Once a physician prescribes a medication, the patient typically fills the prescription at a pharmacy. Pharmacies represent the last link in the supply process prior to pharmaceuticals reaching patients, and their primary function is to dispense medication to patients.[24] Pharmacies typically purchase medications through wholesalers, though they may also acquire medications directly from manufacturers.[25] Pharmacists are expected to evaluate new prescription orders with concurrent treatments, determine whether medication is improperly prescribed, assess prescription orders for forgery or alteration,[26] and ultimately counsel patients on the safe and effective use of their prescriptions.[27] They must also maintain an adequate stock of pharmaceutical products and facilitate billing and payments for patients participating in group health benefit plans.[28] The DEA mandates that pharmacists assess whether controlled substance prescriptions are written for a legitimate medical purpose in the usual course of professional practice.[29]

C. PBMs and health insurers

31. PBMs are widely utilized administrators of prescription plans for health insurers; nearly 266 million Americans had prescription benefits managed by PBMs, i.e., private/commercial insurance, Medicare Part D, and Managed Medicaid, in 2016.[30] In addition to offering prescription services through contracts with retail pharmacies, some PBMs also offer their own mail-order prescription services, which can help both the health plan and health plan enrollees save on prescription expenditures.[31] PBMs work with health

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[23] The Health Strategies Consulting LLC (2005), p. 26.

[24] Eickelberg (2015), p. 7.

[25] Eickelberg (2015), p. 8.

[26] "Pharmacists: On The Front Lines," U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, https://www.cdc.gov/drugoverdose/pdf/Pharmacists_Brochure-a.pdf, last accessed May 2019.

[27] The Health Strategies Consulting LLC (2005), p. 9.

[28] The Health Strategies Consulting LLC (2005), p. 9.

[29] "Pharmacists: On The Front Lines," U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, https://www.cdc.gov/drugoverdose/pdf/Pharmacists_Brochure-a.pdf, last accessed May 2019.

[30] "Pharmacy Benefit Managers (PBMs): Generating Savings for Plan Sponsors and Consumers," Visante, February 2016, p. 3.

[31] "Federal Employees' Health Benefits - Effects of Using Pharmacy Benefit Managers on Health Plans, Enrollees, and Pharmacies," U.S. General Accounting Office, January 2003, p. 4.

insurers to decide which medications will be covered, negotiate how much those medications will cost, and how the costs will be shared between consumers and health insurers, and also help determine costs by negotiating rebates and discounts, participating in formulary development, and establishing pharmacy networks.[32] PBMs offer many other services as well, including claims processing and adjudication, record keeping, reporting programs, helping patients adhere to their prescription regimens, and others.[33]

32. Health insurers in the U.S. provided healthcare coverage for 294.6 million people in 2017.[34] This includes individuals covered by private insurers like Aetna, BCBS, and Kaiser, as well as those covered through government programs such as Medicaid and Medicare.[35] Health insurers provide coverage for a variety of services including preventative care, physician office visits, hospital stays, and prescription medications.[36]

33. Health insurers have considerable insight into a patient's mental and physical health history, because the medical services "purchased" by a patient are submitted as claims by the providers for reimbursement. These claims are routinely reviewed and approved by insurers' claim administrators.[37] Health insurers have the ability to see which doctors a patient visited, what he/she was diagnosed with, and what types of treatments were prescribed, including prescription details.[38] Insurers' vantage point concerning members' medical history is unique. According to the CEO of America's Health Insurance Plans: "Insurance providers have a 360-degree view into care, meaning that they interact with virtually every party involved in a patient's treatment. That means that insurance providers are well positioned to… coordinate patients' care with all of the various entities involved in our health care system…."[39]

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[32] The Health Strategies Consulting LLC (2005), pp. 13–14.

[33] The Health Strategies Consulting LLC (2005), pp. 14–15.

[34] "Health Insurance Coverage in the United States: 2017," U.S. Census Bureau, Economics and Statistics Administration, U.S. Department of Commerce, September 2018 ("U.S. Census Bureau (2018)"), p. 1.

[35] "Health Insurance Market Overview - State Public Health Leadership Webinar," Deloitte, August 15, 2013 ("Deloitte (2013)"), p. 37; U.S. Census Bureau (2018), p. 1.

[36] Deloitte (2013), p. 8.

[37] "Your Simple Guide to Understanding the (Not-So-Simple) Health Insurance Claims Process," *Anthem*, April 13, 2018, https://www.anthem.com/ca/blog/health-insurance-basics/health-insurance-claims-process/; "Insurers Are Well-Positioned To Address Opioid Epidemic," *AHIP*, October 25, 2018, https://www.ahip.org/insurers-are-well-positioned-to-address-opioid-epidemic/.

[38] Torrey, T., "Prescription History and Cost of Health Insurance," *VeryWellHealth*, February 19, 2018.

[39] "Insurers Are Well-Positioned To Address Opioid Epidemic," *AHIP*, October 25, 2018, https://www.ahip.org/insurers-are-well-positioned-to-address-opioid-epidemic/.

34. Health insurers also maintain formularies. Formularies are tools used to control costs by defining which medications will be covered, at what costs, and in what circumstances.[40] Formularies distinguish between preferred and non-preferred products by dividing medications into "tiers," each with a different level of patient cost sharing. The application of formularies to medication selection "is similar to the application of medical treatment guidelines (used by medical specialty groups, health care providers, and insurers) to decisions about treatment regimens."[41] Which medications are covered at which tiers on these formularies "directly or indirectly impact every prescriber, pharmacist, and patient."[42] Indeed, one of Plaintiffs' health economics experts agrees with this view.[43]

35. Health insurers can use a variety of devices to control the circumstances in which opioid medications can be prescribed, including by placing the medications on more expensive tiers or not including the medications at all on the formulary. These steps increase the cost to the patient of certain medications and tend to affect physicians' and patients' utilization of the affected product.

36. Importantly, formulary status and insurance coverage represent an important factor impacting prescribing that Dr. Rosenthal has not incorporated into her model. As I discuss further below, formularies can "can unquestionably exert a powerful influence on prescribing decisions and medication utilization,"[44] and as a result ultimately impact patient outcomes.[45] In this regard, the economic literature documents the substantial growth in the fraction of prescription costs paid by insurance over the period of her analysis. In particular, in 1995, 38 percent of total prescription medication expenditures were paid out of pocket by consumers (e.g. co-pays or paying full price), whereas by 2008 this fraction had declined to just over 20 percent, so that public and private insurance accounted for 80 percent of all prescription medication expenditures in that year.[46]

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[40] "Health Policy Brief: Formularies," Health Affairs, September 14, 2017 ("Health Affairs (2017)"), p. 1.

[41] "Health Affairs (2017), p. 1.

[42] Schiff, G., et al. (2012), "A Prescription for Improving Drug Formulary Decision Making," *PLoS Medicine*, 9(5), pp. 1–7 ("Schiff (2012)"), p. 1.

[43] Deposition of Thomas McGuire on April 30, 2019 ("McGuire Dep."), 786:3–5.

[44] Schiff (2012), p. 1.

[45] Park, Y., et al. (2017), "The Effect of Formulary Restrictions on Patient and Payer Outcomes: A Systematic Literature Review," *Journal of Managed Care and Specialty Pharmacy*, 23(8), pp. 893–901 ("Park (2017)"), p.893.

[46] Pauly, M. (2012), "Insurance and Drug Spending," in *The Oxford Handbook of the Economics of the Biopharmaceutical Industry*, P. Danzon, S. Nicholson, eds. Oxford University Press, Inc., pp. 336–364, p. 349.

D. The FDA and DEA regulate prescription opioid sales, marketing, and distribution practices

37. The FDA's mission includes "ensuring the safety, efficacy, and security of human and veterinary medications, biological products, and medical devices."[47] As part of this mission, the FDA is responsible for approving pharmaceutical medications, monitoring their safety and efficacy while they are on the market, and reviewing and approving marketing materials used in the promotion and advertisement of the pharmaceutical medications to ensure they are truthful and balanced.[48]

38. Among other things, the FDA has specific requirements for prescription product labeling. The primary purpose of labels is to give healthcare professionals the information they need to prescribe medication appropriately.[49] The labels include detailed information on indication and usage, dosage and administration, contraindications, warnings and precautions, interactions, and adverse reactions among others.

39. Additional requirements apply to certain products, including prescription opioid medications. For example, the FDA requires safety monitoring for certain pharmaceutical products through Risk Evaluation and Mitigation Strategy ("REMS") programs.[50] While the elements of different REMS programs may vary, such elements can include, for example, requirements that a manufacturer communicate directly with providers, pharmacists, and nurses about a specific, serious risk associated with a medication and recommended steps to reduce the risk.[51] The FDA can also require the manufacturer to inform patients how to use a medication and avoid serious adverse events. The FDA has determined that a "REMS is necessary for all opioid analgesics intended for outpatient use to ensure that the benefits of these medications continue to outweigh the risks."[52]

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[47] "What We Do," FDA, https://www.fda.gov/aboutfda/whatwedo/default.htm, last accessed May 2019.

[48] "Background on Drug Advertising," FDA, https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm071964.htm, last accessed May 2019.

[49] "An Introduction to the Improved FDA Prescription Drug Labeling," FDA, https://www.fda.gov/downloads/training/forhealthprofessionals/ucm090796.pdf, p. 7, last accessed May 2019.

[50] "Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)," FDA, https://www.fda.gov/drugs/information-drug-class/opioid-analgesic-risk-evaluation-and-mitigation-strategy-rems, accessed May 2019.

[51] "What's in a REMS?" FDA, January 26, 2018, https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592636.htm, last accessed May 2019.

[52] "Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)," FDA, https://www.fda.gov/drugs/information-drug-class/opioid-analgesic-risk-evaluation-and-mitigation-strategy-rems , accessed May 2019.

40. The FDA approved Endo's REMS for reformulated Opana ER in 2011. In 2012, the FDA approved a single REMS for all extended-release and long-acting ("ER/LA") opioid analgesics. For this program, Endo is required to provide to the FDA a medication guide, annual assessment reports, and Elements to Assure Safe Use for healthcare professionals.[53]

41. To the extent that FDA believes the risks outweigh the benefits of any pharmaceutical medication, the FDA can revoke its approval.[54] In situations where the FDA continues to believe that benefits outweigh the risks associated with a medication but risks are high, the FDA can impose "black box" warnings on labels.[55] Prescription opioids are FDA-approved, i.e., they have been subject to the rigorous FDA approval process and have been granted approval for medical use.

42. Similarly, manufacturers of pharmaceutical medications may choose to voluntarily implement a Risk Minimization Action Plan ("RiskMAP") designed to mitigate risks associated with pharmaceutical products.[56] According to the FDA, RiskMAPs use tools such as targeted education and outreach programs, reminder systems, and performance-linked access systems to achieve specific goals and objectives designed to minimize risks while preserving the benefits of the medication.[57] For example, as part of the original Opana ER's FDA approval in 2006, Endo submitted and received approval for a RiskMAP.[58] Endo's 2006 RiskMAP Update Report for Opana ER lists various initiatives to mitigate risk including sales force training, oversight of distribution chain, post marketing surveillance, and formation of a Risk Management Team to review product complaints and adverse events, conduct media surveillance, and analyze market data.[59]

43. For each of Endo's prescription opioid medication, the label communicating the indication and usage has included a warning of the risks involved with the product.[60] This

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[53] Endo Form 10-K for the year ending December 31, 2013, filed June 30, 2013.

[54] "Types of FDA Enforcement Actions," FDA, https://www.fda.gov/animal-veterinary/resources-you/types-fda-enforcement-actions, last accessed May 2019.

[55] "A Guide to Drug Safety Terms," Consumer Health Information, November 2012, p. 2.

[56] *See*, "Guidance for Industry: Development and Use of Risk Minimization Action Plans," U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), March 2005.

[57] *See*, "Guidance for Industry: Development and Use of Risk Minimization Action Plans," U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), March 2005.

[58] "Regulatory History of Opana ER," U.S. Food and Drug Administration, March 13–14, 2017, p. 8.

[59] "RiskMAP Update Report for OPANA ER (oxymorphone hydrochloride) Extended-release Tablets," Endo Pharmaceuticals Inc., March 2007, ENDO_CHI-NY-SUB_ESI_040_00029445.

[60] "Opana ER," July 2006, p. 1.

was the case throughout the years at issue in this litigation, and across multiple products.[61] These labels for Endo's products have included known risks, such as the potential for abuse, and the unknown risks or possible benefits, such as the effect of the prescription medication on the immune system.[62]

44. Further regulation exists throughout the prescription opioid supply chain. While the FDA approves prescription opioids, monitors their use for safety and efficacy, and approves manufacturers' marketing materials, the DEA monitors the sales and distribution of these opioids through its Automation of Reports and Consolidated Orders System ("ARCOS") program.[63]

45. The DEA limits the supply of opioids through annual production quotas the agency establishes for each controlled substance in schedules I and II as well as some other medications.[64] The DEA sets these quotas considering estimates of medical need from the FDA, prescription rates, historical data from manufacturers, internal DEA data on controlled substances, and historical quota levels.[65] The intent of these quotas is to "provide for the adequate and uninterrupted supply for legitimate medical need of the types of schedule I and II controlled substances that have a potential for abuse, while limiting the amounts available to prevent diversion."[66] These quotas held constant from 2008 through 2012, increased in 2013, began to gradually decrease in 2015, and declined sharply in 2017, as shown in Figure 2.

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[61] *See,* ENDO-OPIOID_MDL-05411874–879 at 875 ("Percocet," September, 1997); "Opana ER," July 2006, p. 1; "Opana ER," September 2010, p. 1; ENDO-OPIOID_MDL-05532549–554 at 549 ("Supplement Approval: Percocet," August 18, 2013).

[62] "Opana ER," July 2006, pp. 1, 3; "Opana ER," September 2010, pp. 1, 16.

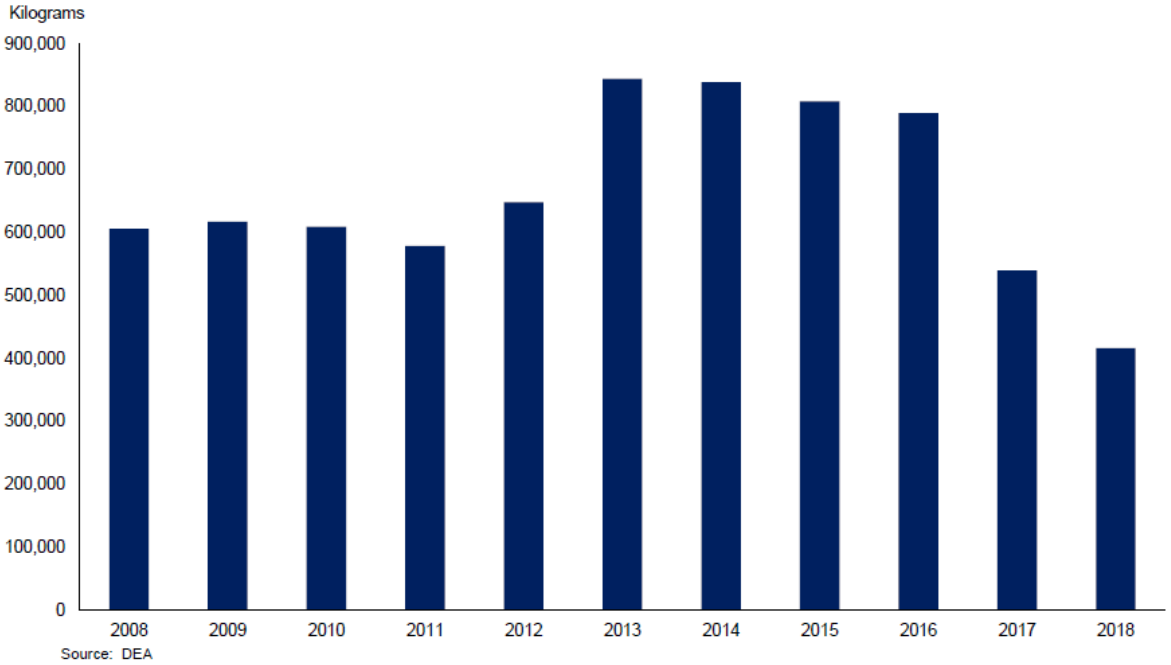
[63] "Step 5: FDA Post-Market Drug Safety Monitoring," FDA , https://www.fda.gov/patients/drug-development-process/step-5-fda-post-market-drug-safety-monitoring, last accessed May 2019; "Automation of Reports and Consolidated Orders System (ARCOS)," DEA, https://www.deadiversion.usdoj.gov/arcos/index.html, last accessed May 2019.

[64] "Title 21 United States Code (USC) Controlled Substances Act: Subchapter I - Control and Enforcement," Diversion Control Division, DEA, U.S. Department of Justice.

[65] "DEA Reduces Amount of Opioid Controlled Substances to Be Manufactured in 2017," DEA, October 4, 2016 ("DEA (2016)").

[66] DEA (2016).

Figure 2. DEA Absolute Production Quotas of Schedule II Opioids, 2008-2018



Source: DEA

Note: Schedule II opioids include alfentanil, codeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, opium, oripavine, oxycodone, oxymorphone, sufentanil, thebaine, and tapentadol. Production quotas include substances for sale and for conversion. Sale quotas apply to substances that will retain their basic drug class, whereas conversion quotas apply to substances that that will be converted to a different basic drug class, such as from morphine to hydromorphone.

V. DR. ROSENTHAL MISSTATES THE ROLE AND IMPACT OF PHARMACEUTICAL MARKETING

46. Dr. Rosenthal's description of the impact of marketing activities in pharmaceutical markets is flawed and results in Dr. Rosenthal overstating the impact of pharmaceutical detailing on prescription opioid sales. Dr. Rosenthal fails to account for numerous other factors that are unrelated to marketing but impact physician prescribing decisions. Further, she makes a series of flawed assumptions regarding the marketing activities in the pharmaceutical industry, rendering the foundation of her statistical framework flawed and unreliable. I discuss these issues with Dr. Rosenthal's analysis in detail below.

47. Pharmaceutical marketing can serve a legitimate purpose: it is used by manufacturers to convey information about the availability and attributes of their products, mostly to physicians. But marketing is just one of many factors physicians consider when making prescribing decisions. Dr. Rosenthal claims that as many as [redacted] percent of MMEs were attributable to the Manufacturer Defendants' detailing in a given year.[67] This result is

[67] Rosenthal Report, Table 2.

implausible and not supported by any reliable analysis. There are numerous other factors that impact prescribing decisions, most of which are more impactful than the detailing by pharmaceutical manufacturers. Dr. Rosenthal ignores the impact of all of these other factors on physician prescribing and attributes all changes in physician prescribing behavior to manufacturers' detailing activities. Moreover, Dr. Rosenthal has not considered the additional sources of information about prescription opioids when she evaluates the role of detailing on prescription opioid shipments. This omission is another reason why Dr. Rosenthal's opinions are unreliable.

A. Dr. Rosenthal fails to account for various factors that influence physician prescription decisions

48. The decision to prescribe a medication to a patient is highly individualized: Physicians make prescription decisions based on each patient's individual needs.[68] Physicians are influenced by many factors when making prescription decisions. The literature identifies a number of factors beyond marketing and promotion that are known to affect prescribing choices. These include cost of medicine, patients' clinical condition and preference, attributes of the available treatment options, the physician's training and experiences, insurance coverage, and formulary placement.[69]

49. Studies that assess factors impacting prescribing decisions highlight the roles of physicians' attributes including specialty, experience, and location.[70] Studies have also found that physicians are primarily influenced by their prior experiences.[71] In particular, physicians typically closely monitor side effects and patient satisfaction for medications new to the market, and attempt to learn about effectiveness by examining performance in their patients,

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[68] Gallan, A. (2004), "Factors that Influence Physicians' Prescribing of Pharmaceuticals: A Literature Review," Journal of Pharmaceutical Marketing and Management, 16(4), pp. 3–46 ("Gallan (2004)"), p. 8; Schumock, G., et al (2004), "Factors that Influence Prescribing Decisions," *The Annals of Pharmacotherapy*, 38(4), pp. 557–562 ("Schumock (2004)"), p. 561; Thompson, M. (1997), "Characteristics of Information Resources Preferred by Primary Care Physicians," Bulletin of the Medical Library Association, 85(2), pp. 187–192 ("Thompson (1997)"), p. 187; Venkataraman, S. and Stremersch, S. (2007), "The Debate on Influencing Doctors' Decisions: Are Drug Characteristics the Missing Link?" *Management Science*, 53(11), pp. 1688–1701 ("Venkataraman (2007)"), p. 1700; Sirovich, B., et al (2008), "Discretionary Decision Making by Primary Care Physicians and the Cost of U.S. Health Care," *Health Affairs*, 27(3), pp. 813–823 ("Sirovich (2008)").

[69] *See*, Gallan (2004); Schumock (2004); Thompson (1997); Venkataraman (2007).

[70] *See,* Chandra, A. and Staiger, D. (2007), "Productivity Spillovers in Health Care: Evidence from the Treatment of Heart Attacks," *Journal of Political Economy*, 115(1), pp. 103–140; Sirovich (2008); Sommers, B., et al (2008), "Predictors of Patient Preferences and Treatment Choices for Localized Prostate Cancer," *Cancer*, 113(8), pp. 2058–2067.

[71] Spiller, L. and Wymer, W. (2001), "Physicians' Perceptions and Uses of Commercial Drug Information Sources: An Examination of Pharmaceutical Marketing to Physicians," *Health Marketing Quarterly*, 19(1), pp. 91–106, p. 91.

which in turn influences the likelihood the physician will prescribe that medication for future patients.[72] Similarly, physicians regularly engage in ongoing medical education throughout their entire careers, and for many physicians this ongoing education serves as an important source of information for their prescribing choices.[73]

50. Furthermore, physicians prioritize scientific information such as results of clinical trials and demonstrated results in peer-reviewed journals,[74] as well as medical textbooks[75] over the other sources of information such as journal advertisements or detailing visits. For example, the Physicians' Desk Reference is an annually published (though now available online) reference guide of prescribing information for branded medicines.[76] Endo products appeared in the Physicians' Desk Reference, with detailed indication and usage information, throughout the years of the alleged conduct.[77] While Dr. Rosenthal cites to the report of another Plaintiff expert, Dr. Mathew Perri, in order to assert that "[p]hysicians may not be able to easily discriminate between promotional information and scientific evidence,"[78] the works cited to support that statement consist of: (1) a study conducted in Australia and Malaysia in which physicians, contrary to Dr. Rosenthal's claim, *correctly* identified when contraindications or precautions were omitted from detailing visits; and (2) a 1995 survey based on a sample of only 27 physicians.[79] Neither study evaluated prescribing decisions or outcomes for prescription opioids.

51. Prescription decisions are also impacted by other health care entities such as hospitals, PBMs, and health insurers who manage formularies using mechanisms, such as prior

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[72] *See, e.g.*, Chintagunta, P., Jiang, R., and Jin, G. (2009), "Information, Learning, and Drug Diffusion: the Case of Cox-2 Inhibitors," *Quantitative Marketing and Economics*, 7(4), pp. 399–443.

[73] "AMA Code of Medical Ethics," *American Medical Association*, https://www.amaassn.org/sites/default/files/media-browser/principles-of-medical-ethics.pdf, last accessed May 2019; Bennett, N., et al (2004), "Physicians' Internet Information-Seeking Behaviors," *The Journal of Continuing Education in the Health Professions*, 24(1), pp. 31–38, p. 31.

[74] Gallan (2004); Azoulay, P. (2002), "Do Pharmaceutical Sales Respond to Scientific Evidence?" *Journal of Economics and Marketing Strategy,* 11(4), pp. 551–594 ("Azoulay (2002)").

[75] *See*, *e.g.*, Andrews, J., et al (2005), "Information-Seeking Behaviors of Practitioners in a Primary Care Practice-Based Research Network," *Journal of the Medical Library Association*, 93(2), pp. 206–212; Spiller, L. and Wymer, W. (2002), "Physicians' responses to Marketing Strategies of Pharmaceutical Companies," *Journal of Pharmaceutical Marketing and Management*, 15(1), pp. 15–30.

[76] "About PDR Network," Prescribers' Digital Reference, https://www.pdr.net/about-pdr-network/, last accessed May 2019.

[77] *See,* PDR Staff, "Percocet," in *1995 Physicians' Desk Reference*, 49th Edition (1995); PDR Staff, "Percocet," in *2008 Physicians' Desk Reference*, 62nd Edition (2008).

[78] Rosenthal Report, ¶ 30.

[79] Othman, N., et al (2010), "Medicines [sic] Information Provided by Pharmaceutical Representatives: A Comparative Study in Australia and Malaysia," *BMC Public Health*, 10(743), pp. 1–11, p. 8; Ziegler, M., Lew, P., Singer, B. (1995), "The Accuracy of Drug Information from Pharmaceutical Sales Representatives," *JAMA*, 273(16), pp. 1296–1298, p. 1296.

authorizations, to dictate or influence the circumstances in which certain medications may be prescribed.[80]

52. By "identifying, weighing, and designating best evidence, formularies can assess, teach, and guide prescribing toward the most appropriate and evidence-based choices, helping to direct use toward the most efficacious, safest, and cost-effective therapies, while serving as a firewall to protect against prescribing overly driven by marketing claims."[81] Thus, "formularies can unquestionably exert a powerful influence on prescribing decisions and medication utilization,"[82] and as a result ultimately impact patient outcomes.[83] Another one of Plaintiffs' experts, Dr. Thomas McGuire, acknowledges the importance of formularies by stating that "it [is] part of the intention of formularies to influence not just patients but to influence doctors in what they recommend. And, yes, formularies can affect selection of drugs."[84]

53. Dr. Rosenthal has not incorporated into her model any of these factors, including physicians' attributes, formulary status or insurance coverage, even though all of these factors impact physician prescription decisions and hence drive the prescribing that she analyzes in her report.

54. Moreover, Dr. Rosenthal has not considered additional sources of information that might impact physicians' decision to prescribe opioid medications. These factors and additional sources of information include press coverage (which has been significant, including publicity regarding alleged improper marketing of certain opioids), clinical studies, medical journals, FDA-approved labeling and labeling changes and black box warnings, changing CDC guidelines, and DEA's "threat assessment" reports and production quotas on controlled substances.

55. For example, according to a study published in 2016, between 1998 and 2012, there were 4,625 national newspaper stories in the U.S. and 654 television stories that included content about opioid analgesic abuse, addiction or dependence. Drawing from a random

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[80] "Prior authorizations" are approvals needed by a health insurance carrier for certain medications before the insurer will cover them. *See*, "What is Prior Authorization and How Does the Process Work?" *Cigna*, July 2018, https://www.cigna.com/individuals-families/understanding-insurance/what-is-prior-authorization, last accessed May 2019.

[81] Schiff (2012), p. 1.

[82] Schiff (2012), p. 1.

[83] Park (2017), p. 893.

[84] McGuire Dep., 763:21–764:1.

sample of these stories, the study found that 94 percent of the news media stories mentioned a health-related consequence of opioid analgesic abuse.[85] Addiction or dependence was mentioned most frequently (75%), followed by death (53%) and overdose (41%).[86] During the same time period, there were numerous Congressional hearings on the same subject, with topics such as "OxyContin: Balancing Risks and Benefits,"[87] "OxyContin: Its Use and Abuse,"[88] "To Do No Harm: Strategies for Preventing Prescription Drug Abuse,"[89] "OxyContin and Beyond: Examining the Role of FDA and DEA in Regulating Prescription Painkillers,"[90] "Prescription Drug Abuse: What Is Being Done to Address This New Drug Epidemic?,"[91] and "Drug Waste and Disposal: When Prescriptions Become Poison."[92]

B. Other factors and sources of information are more important than pharmaceutical marketing in driving physician prescription decisions

56. While detailing to physicians may have an impact on physician prescribing decisions,[93] it is consistently rated as less important than other factors (such as other information sources I discussed above, or the cost of the medication), even when advertisements appear in medical journals. One study found that detailing, advertisements distributed by sales representatives, advertisements in medical or professional journals, and displays at professional meetings were all rated as substantially less important factors than effectiveness and safety, prescribing guidelines, and formulary status.[94] Most surveyed physicians indicate that "commercial sources of information are less influential than scientific

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[85] "Criminal Activity or Treatable Health Condition? News Media Framing of Opioid Analgesic Abuse in the United States, 1998–2012," *The American Journal of Psychotherapy*, 67(4), p. 405–411.

[86] "Criminal Activity or Treatable Health Condition? News Media Framing of Opioid Analgesic Abuse in the United States, 1998–2012," *The American Journal of Psychotherapy*, 67(4), p. 405–411.

[87] "OxyContin: Balancing Risks and Benefits," National Institute on Drug Abuse, February 12, 2002.

[88] "OxyContin: Its Use and Abuse," Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives, August 28, 2001.

[89] "To Do No Harm: Strategies for Preventing Prescription Drug Abuse," Committee on Government Reform, House of Representatives, February 9, 2004.

[90] "OxyContin and Beyond: Examining the role of FDA and DEA in Regulating Prescription Painkillers," Committee on Government Reform, House of Representatives, September 13, 2005.

[91] "Prescription Drug Abuse: What Is Being Done to Address This New Drug Epidemic?" *Health Policy Review*, 9, pp. 287–321.

[92] "Drug Waste and Disposal: When Prescriptions Become Poison," Special Committee on Aging, United States Senate, June 30, 2010.

[93] Gallan (2004), p. 9.

[94] Schumock (2004), p. 558.

literature."[95] Quantitative analyses further demonstrate that while effects of detailing and sampling are positive and statistically significant, the magnitudes of these effects are small.[96]

57. In summary, Dr. Rosenthal assumes that physicians prescribing decisions were determined primarily by manufacturers' allegedly deceptive detailing messages,[97] and that physicians were either unaware of or rejected the widely-available, public information concerning prescription opioids summarized above. Dr. Rosenthal also ignores the impact on prescribing behavior of relevant factors such as the cost of medicine, patients' clinical condition and preference, attributes of the available treatment options, the physician's training and experiences, insurance coverage, and formulary placement. These assumptions are unfounded and implausible and render her opinions unreliable.

VI. DR. ROSENTHAL'S METHODS FOR EVALUATING THE CAUSAL IMPACT OF PRESCRIPTION OPIOID MANUFACTURERS' MARKETING REST UPON FUNDAMENTALY FLAWED ASSUMPTIONS REGARDING THE NATURE OF PHARMACEUTICAL MARKETING

58. Dr. Rosenthal makes a series of flawed assumptions regarding the marketing activities in the pharmaceutical industry, rendering the foundation of her statistical framework flawed and unreliable. For example, Dr. Rosenthal assumes that all prescription opioids are the same, that detailing is the only relevant form of marketing, that each instance of physician detailing has a market expanding effect, and that each instance of detailing has comparable effects (without regard to, for instance, the product or company involved or the content of the communication). While each assumption would on its own lead to biased conclusions, the combination of all of these assumptions renders the foundation of Dr. Rosenthal's framework flawed and unreliable.

A. Dr. Rosenthal inappropriately assumes all prescription opioid medications are the same and each instance of detailing has the same effect on prescribing

59. Dr. Rosenthal creates her model using national level data that aggregates prescription opioid shipments and prescription opioid detailing across all Defendant Manufacturers. This

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[95] Gallan (2004), p. 9.

[96] Mizik, N. and Jacobson, R. (2004), "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science*, 50(12), pp. 1704–1715 ("Mizik (2004)"), p. 1704.

[97] The only other determinant of prescription opioid MMEs in Dr. Rosenthal's model is price.

aggregate approach to estimation in effect assumes that all prescription opioid medications are the same and each instance of detailing has the same effect on prescribing. However, this assumption is unfounded as it ignores differences among medications, applications both in terms of active ingredients and in terms of uses, geography, physicians, and patients, as well as the content of detailing communications.

60. For starters, there are two categories of prescription opioid medications, long-acting / extended release and short-acting / immediate release. Immediate release opioids "are faster acting medication[s] with a shorter duration of pain-relieving action" and extended release opioids are "slower-acting medication[s] with a longer duration of pain-relieving action."[98] These are two different types of products and often used for different conditions, therefore detailing for one product will not necessarily impact prescriptions for another product.

61. Different opioid medications may compete in different markets. For example, typically immediate release / short acting opioid medications are not used for the same applications as extended release / long acting opioid medications.[99] Even within these broad categories, different medications may not be readily substitutable for one another, or may have different attributes that result in product differentiation.[100]

62. Dr. Rosenthal's decision to lump together all prescription opioids is inconsistent with market realities. Rather than acknowledging that marketing related to one type of prescription opioid, e.g., a short-acting medication, is unlikely to impact shipments of another manufacturer's differentiated prescription opioid, e.g., a long-acting, extended release medication, Dr. Rosenthal glosses over these differences by assuming a single relationship holds between each instance of one manufacturer's marketing and rates of prescribing for all prescription opioids, irrespective of the manufacturer of the product or any of the product's differentiating attributes.

63. Moreover, Dr. Rosenthal estimates her model on a nationwide basis, meaning that Dr. Rosenthal has not only pooled quantities of MMEs across heterogeneous counties, but she has also pooled quantities of detailing across manufacturers who have varied in their marketing messages and prioritization of different geographies. However, the reality of the

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[98] "Commonly Used Terms," U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, https://www.cdc.gov/drugoverdose/opioids/terms.html, last accessed May 2019.

[99] "2009 Opana Brand Plan," *Endo Pharmaceuticals*, 2009, p. 10.

[100] "2009 Opana Brand Plan," *Endo Pharmaceuticals*, 2009, pp. 5, 7–9.

marketplace is that not all marketing is the same and not all manufacturers devote identical amounts of resources to all counties.

B. Dr. Rosenthal ignores the competitive effects of marketing, and instead assumes all detailing has the same market expanding impact on prescription opioids sales

64. Dr. Rosenthal also fails to distinguish between marketing that increases market size and marketing that increases a particular product's market share. Instead, Dr. Rosenthal assumes in her aggregate model approach that all detailing is the same in terms of market expansion effects, and ignores the competitive aspects of marketing designed to increase market share.

65. This distinction between the effects of promotion on market expansion and market share has important implications for Dr. Rosenthal's analysis, which purports to model the relationship between detailing and prescribing. In reality, it is possible, and indeed common, for marketing relating to a certain brand to increase prescribing for that brand at the expense of the competitor's brand, resulting in little or no change in overall prescribing, as compared to what overall prescribing would have been in the absence of that marketing. In fact – and contrary to Dr. Rosenthal's model formulation and results – studies have shown a *negative* impact from rivals' detailing on one's own shipments.[101]

66. Substantial academic literature recognizes that marketing has competitive effects (in that it may change market share – i.e., it would be improper to assume only market expanding effects).[102] These results hold for a variety of pharmaceutical products. Literature on the market for antidepressants, for example, distinguishes between the impact of marketing on market size and its impact on market share.[103] In fact, recent literature has shown that the

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[101] *See,* Azoulay (2002).

[102] *See,* Comanor, W. and Wilson, T. (1979), "The Effect of Advertising on Competition: A Survey," *Journal of Economic Literature*, 17(2), pp. 453–476. Azoulay (2002); Chintagunta, P., Desiraju, R., and Narayanan, S. (2004), "Return on Investment Implications for Pharmaceutical Promotional Expenditures: The Role of Marketing-Mix Interactions," *Journal of Marketing*, 68(4), pp. 90–105.

[103] Berndt, E., et al (2002), "An Analysis of the Diffusion of New Antidepressants: Variety, Quality, and Marketing Efforts," *The Journal of Mental Health Policy and Economics*, 5, pp. 3–19 ("Berndt (2002)"). Other literature has shown this effect for ACE-inhibitors. *See, e.g.*, Ching, A. and Ishihara, M. (2010), "The Effects of Detailing on Prescribing Decisions Under Quality Uncertainty," *Quantitative Marketing and Economics*, 8(2), pp. 123–165.

primary effect of marketing for pharmaceutical medications has been a redistribution of market shares, not an expansion of the market.[104]

VII. DR. ROSENTHAL'S STATISTICAL ANALYSIS SUFFERS FROM A SERIES OF CONCEPTUAL MISTAKES THAT RENDER HER ANALYSES UNRELIABLE

67. Dr. Rosenthal's econometric analysis consists of two approaches. She first considers a "direct approach," purporting to measure directly the relationship between prescribing and detailing.[105] In her model, "excess" prescribing is a function of her estimated impact of detailing. The only other variables Dr. Rosenthal uses in this model are an aggregate prescription opioid price index she constructed herself,[106] and a series of indicator variables corresponding to individual events, such as the release of Joint Commission on Accreditation of Healthcare Organization ("JCAHO") pain standards in January 2001.[107] Dr. Rosenthal ultimately concludes, however, that the model consisting only of detailing and the aggregate price index is a "fair, accurate, and econometrially [sic] sound method by which to estimate the relationship of the Manufacturer Defendants' detailing of prescription opioids on the sales of prescription opioids over the time period 1993-2018."[108]

68. Dr. Rosenthal also uses an "indirect approach," in which she first estimates a relationship between county-level prescribing and a set of economic and demographic controls during a control period of 1997, and then she uses this model to predict county-level prescribing through 2016. Dr. Rosenthal characterizes the differences between her predicted level of MMEs and actual levels as "excess" prescribing, purportedly due to manufacturers' detailing.[109]

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[104] Fischer, M. and Albers, S. (2009), "Patient- or Physician-Oriented Marketing: What Drives Primary Demand for Prescription Drugs?," *Journal of Marketing Research,* 47(1), pp. 103–121, p. 114. ("In summary, the increased investment in detailing and DTC advertising in recent years did not lead to market expansion but rather resulted in a redistribution of market shares.").

[105] Rosenthal Report, Table 1, ¶¶ 49, 74.

[106] Rosenthal Report, Attachment D, p. D4. Dr. Rosenthal's price index is constructed by adding sales across package/strength/forms of prescription opioids and dividing by total quantity. Dr. Rosenthal purports to account for entry and exit in the prescription opioid market by doing this only over package/strength/form/prescription opioid combinations that were present in two consecutive months.

[107] Rosenthal Report, Table 1.

[108] Rosenthal Report, ¶ 74.

[109] Rosenthal Report, ¶¶ 79–82. The controls considered in Dr. Rosenthal's indirect regression method do not include any marketing expenditures, either by Manufacturer Defendants or Manufacturer non- Defendants. Thus, the "indirect approach" fails to even control for whether the detailing at a given point in time was by a Manufacturer Defendant or not, let

69. Dr. Rosenthal uses the results from her direct regression model to estimate the percentage of total MMEs attributable to detailing by the Manufacturer Defendants, and finds that in a given year, as large as [redacted] percent of all prescription opioid shipments were attributable to such detailing.[110] Dr. Rosenthal summarizes her "direct approach" results on the difference between actual MMEs and "the number of MMEs that would have been filled but-for the alleged wrongdoing" in Table 2 of her report.[111] These results are then used as the primary metrics in Dr. David Cutler's and Dr. Thomas McGuire's analyses.[112] Using the same direct regression model, Dr. Rosenthal also attempts to show "the impact of manufacturer misconduct on MMEs from 1995-2018 while assuming the promotion by one Defendant at a time is deemed lawful," summarizing her results in Table 3.[113]

70. Since Dr. Rosenthal's statistical framework is flawed and cannot be used reliably to address the relationship between detailing and prescription opioid shipments, the results she reports in Table 2 (and that Dr. Cutler and Dr. McGuire rely on for their own analyses) and Table 3 are also flawed and unreliable.[114] Thus, Dr. Rosenthal fails to provide a reliable basis for analyzing the effects of the alleged deceptive marketing practices on the prescription opioid market. Because of these errors, Dr. Rosenthal's analysis cannot be used to show that detailing of prescription opioid medications by pharmaceutical manufacturers led to "excess" prescribing.

A. Dr. Rosenthal's statistical framework is not designed to measure causality, and is instead only a data fitting exercise with numerous flaws

71. Dr. Rosenthal claims her econometric methodology is able to "quantify directly the causal relationship between promotion and sales."[115] However, Dr. Rosenthal's modeling

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alone whether it was unlawful. I therefore find Dr. Rosenthal's indirect regression approach even less reliable than her direct regression.

[110] Rosenthal Report, ¶ 75, Table 2.

[111] Rosenthal Report, ¶ 75.

[112] Expert Report of Professor David Cutler, dated March 25, 2019 ("Cutler Report"), ¶ 9; Expert Report of Professor Thomas McGuire, dated March 25, 2019 ("McGuire Report"), ¶ 15. Dr. Cutler and Dr. McGuire also consider Dr. Rosenthal's indirect regression results, but relegate these considerations to appendices. Cutler Report, n.7; McGuire Report, n.14.

[113] Rosenthal Report, ¶ 76, Table 3.

[114] Dr. Rosenthal describes Table 3 as follows in her report: "Table 3 shows the impact of manufacturer misconduct on MMEs from 1995-2018 while assuming the promotion by one Defendant at a time is deemed lawful (and therefore is allowed to generate prescriptions in the but-for scenario). *See*, Rosenthal Report, ¶ 76. Furthermore, Dr. Rosenthal testified in her deposition that "the purpose of Table 3 is to show that I can back out individual levels of detailing, not to assign liability." Deposition of Meredith Rosenthal on May 4, 2019 ("Rosenthal Dep."), 164:10–12.

[115] Rosenthal Report, ¶ 10.

practices are fundamentally designed to achieve artificially good model fit and cannot identify any causal relationship between prescription opioid shipments and detailing. There are several key flaws in Dr. Rosenthal's modeling that are inconsistent with standard practice and appear to be designed to manipulate the data to achieve artificially good fit.

72. First, even though Dr. Rosenthal's goal is to study the role of all marketing done by pharmaceutical manufacturers, she uses only one type of marketing: detailing.[116] Since Dr. Rosenthal ignores other forms of marketing that might impact physician prescribing, she overstates the importance of detailing on opioid prescribing. Second, Dr. Rosenthal does not use the number of monthly contacts directly in her model. Instead, Dr. Rosenthal creates a new variable she calls the "stock of contacts," which grows at an exponential rate over time.[117] This modeling choice is crucial for Dr. Rosenthal's results, even though it is inconsistent with both standard marketing literature, which finds that marketing messages decay over time, and the realities of the pharmaceutical marketplace, in which new physicians enter every year who have not been exposed to past marketing messages.

73. Another problem with Dr. Rosenthal's model is her arbitrary imposition of two "structural breaks."[118] Specifically, Dr. Rosenthal first identifies a change in the impact of detailing on MMEs in March 2002, and then she identifies a second change in the impact of detailing in August 2010.[119] However, Dr. Rosenthal's use of these "breaks" is nonsensical and unsupported. Dr. Rosenthal, without explanation, models the first structural break as a change in the level of impact of detailing, and models the second structural break as a change in the trend of impact of detailing. Dr. Rosenthal does not provide any explanation as to why events associated with each break would have different manifestations in her model. Dr. Rosenthal's use of a trend break in August 2010 is, presumably, to ensure that the effect of the stock of contacts in her model will more closely trace the downward trend in total MMEs.[120] However, Dr. Rosenthal offers no explanation as to why the changes taking place in or around August 2010 that reduced total MMEs would manifest as a change to the impact of detailing instead of a change to the market itself. A more sensible approach would be to

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[116] Rosenthal Report, ¶ 56.
[117] Rosenthal Report, ¶ 61.
[118] Rosenthal Report, ¶ 65.
[119] Rosenthal Report, Table 1.
[120] Rosenthal Report, Figure D.2.

use an independent time trend to reflect potential decreases in overall supply and demand for prescription opioid medications. Dr. Rosenthal's choice is a nonsensical modeling decision that violates standard econometric principles, and is also a crucial assumption for Dr. Rosenthal's results. Fourth, other than the stock of contacts, the only other factor Dr. Rosenthal uses in her direct model is a price index that she created herself.[121] There is no variable in the model to capture all the other relevant factors that might lead to changes in prescribing levels, such as socioeconomic and demographic conditions, general healthcare spending trends, or geographical variances.[122] Fifth, Dr. Rosenthal uses total MMEs as a proxy for prescription opioid sales, but she does not check whether her results are robust, i.e. whether the results would have changed if she had used other, potentially more appropriate measures of the size of the market such as number of prescriptions or number of patients.[123]

74. As a result, Dr. Rosenthal ends up modeling total prescribing (measured in MMEs) as a complicated, unconventional, time-varying function of detailing activity. What Dr. Rosenthal has actually accomplished is to bend and twist her measure of detailing, i.e., the stock of contacts variable she devises, until it approximates total MMEs as closely as possible, artificially achieving good model fit instead of measuring a causal relationship. This approach is inconsistent with standard use of statistical modeling and best practices. A valid empirical model needs to specify precise relationships among demand and supply factors for the particular aspect of the economy being studied, consider broader economic conditions, and be consistent with economic theory.[124]

75. Figure 3 presents graphically the implausible implications of Dr. Rosenthal's approach. Using Dr. Rosenthal's model and results, but applying it to a single physician rather than in the abstract aggregate, Dr. Rosenthal's analysis implies that a single detailing visit in 1995 can have *both increasing and decreasing effects* on a physician's prescription

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[121] Rosenthal Report, Attachment D, p. D4.

[122] *See, e.g.*, Wooldridge, J. (2009), "Causality and the Notion of Ceteris Parabus in Econometric Analysis," in *Introductory Econometrics A Modern Approach*, South-Western Cengage Learning, pp. 12–17.

[123] For example, Dr. Rosenthal cannot discern in her model whether a smaller number of patients are increasingly misusing prescription opioids, or if a larger number of patients are receiving clinically-suggested dosages. Rosenthal Dep., 172:3–16 ("Q. So you could have one patient taking 100 MMEs over the course of ten days and ten patients taking ten MMEs over the course of the same period of time, and your model makes no distinction between those two circumstances? A. Yes, that's correct. Again, because I am -- I am responsible for looking at the effect of marketing on sort of the quantity of morphine equivalence that were out in the world. Whereas Professor Cutler is then going to look at the effect of those MMEs on harms, and his model will establish the relationship between MMEs and harms.").

[124] Greene, W. (2012), "The Classical Multiple Linear Regression Model," *Econometric Analysis*, Prentice Hall, pp. 7–18, p. 7.

habits. In other words, Dr. Rosenthal's results imply that: (1) if a representative physician was visited only once by a Manufacturer Defendant representative in January 1995, the immediate impact of the detailing visit is to increase opioid prescriptions by 933 MME that month; and (2) 15 years later, in January 2010, with no additional detailing visits, the representative physician prescribes an additional 3,710 MMEs that month, due to single detailing visit *from 1995*. The 3,710 MMEs in January 2010 resulting from the January 1995 detailing visit represent an additional 2,777 MMEs relative to the January 1995 detailing visit's immediate impact, even though 15 years have passed.[125]

76. To put this further in perspective, according to Dr. Rosenthal's results, a detailing visit in January 2010 results in 1,111 additional MMEs that month, whereas in January 2010 a single visit from 15 years ago, in 1995, generates more than three times as many MMEs in that same month.[126] Therefore, in January 2010, the 1995 detailing visit is almost four times as powerful as the January 2010 detailing visit. As I discuss further below, not only is this calculation nonsensical on its face, it is impossible to reconcile it with the fact that new physicians are entering the market and/or beginning to prescribe opioid medications every year (*see* Figure 4). It is impossible for this pattern of detailing impact to hold for a physician entering the market in 2010 since he or she would not have heard the 1995 message in the first place.

77. In addition, because Dr. Rosenthal imposes arbitrary structural breaks in her model, the impact of the single January 1995 detailing visit increases over time only to a point. That is, the impact of the January 1995 detailing visit begins to decline after August 2010.[127] This is not due to a positive depreciation rate as observed in the existing literature, but rather the negative trend dummy variable interaction with the stock of contacts in Dr. Rosenthal's model after August 2010.

78. The above nonsensical effect of a January 1995 detailing visit is an artifact of Dr. Rosenthal's modeling choices. The end result of the above is that a single detailing visit from a Defendant Manufacturer, in January 1995 is ultimately, by May 2018, responsible on its own for [redacted] excess MMEs.[128]

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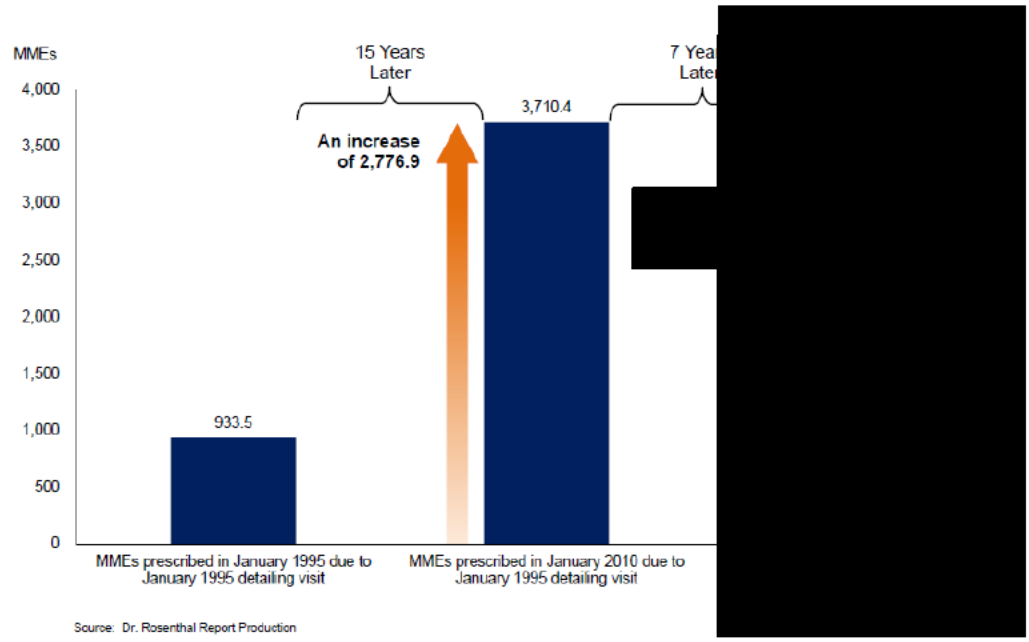
[125] Note that Endo did not come into existence until 1997.

[126] Rosenthal Report, Table 1.

[127] Rosenthal Report, Table 1.

[128] *See* Production backup for Figure 3. This represents the total amount of MMEs Dr. Rosenthal's model would predict were shipped from January 1995 to March 2018 due to the single detailing visit in January 1995. If a Defendant Manufacturer conducted this detailing visit, these MMEs would be deemed by Dr. Rosenthal to be "excess" shipments.

Figure 3. Dr. Rosenthal's Predicted Effect of a Single Detailing Visit in January 1995 on an Individual Doctor's Prescribing Behavior



B. Dr. Rosenthal's results rely on the assumption that all detailing by Manufacturing Defendants was deceptive and unlawful

79. As I explained above, Dr. Rosenthal's stated goal is to "quantify directly the causal relationship between promotion and sales."[129] I already identified numerous issues with her framework in Section VII.A. However, I note that Dr. Rosenthal's framework suffers from a more critical flaw that renders her results on "the percent of MMEs attributable to challenged promotion" unreliable.[130] Specifically, there is no variable in Dr. Rosenthal's "direct model" to identify any of the "challenged promotion" she claims. Instead, Dr. Rosenthal simply assumes all detailing by the Manufacturer Defendants was wrongful.[131]

80. Dr. Rosenthal states that she was instructed by Plaintiffs' counsel to "assume in [the] but-for scenarios that the fact finder (judge or jury) finds that all or virtually all promotion by the [M]anufacturer Defendants from 1995 to the present was unlawful."[132] The implication

[129] Rosenthal Report, ¶ 10.
[130] Rosenthal Report, Table 2.
[131] Rosenthal Report, ¶ 61.
[132] Rosenthal Report, ¶ 75.

of this assumption is that in Plaintiffs' but-for world, there would have been *no* promotion by any Manufacturer Defendant, for *any* prescription opioid, from 1995 through present. This assumption is inconsistent with the nature and history of the pharmaceutical industry and pharmaceutical marketing in general. As I described in Section IV, pharmaceutical manufacturing, distribution, and marketing are highly regulated and frequently scrutinized. Prescription opioid medications are no different from any other FDA-approved pharmaceutical in these aspects. Marketing prescription opioid medications, including through meetings with physicians, is legal in the U.S., and the FDA oversees and governs those practices, including the approval of marketing messages, materials, and physician communications.[133]

81. Furthermore, Dr. Rosenthal claims that her model can be adjusted in the event a fact finder concludes that some detailing by Manufacturer Defendants was lawful.[134] She does not describe precisely how she would go about accomplishing this task, but if the calculations in her Table 3 are any indication, it is reasonable to presume that if a fact finder concludes that 10 percent of such detailing was misleading, Dr. Rosenthal would reassign 90 percent of Manufacturer Defendants detailing as lawful in her calculation of "excess" prescribing. This assumes that there is a linear, aggregate relationship between prescription opioid MMEs and pharmaceutical detailing that is the same across Manufacturer Defendants and products, and over time. However, if firms and brands differ in terms of market expansion versus market sharing impacts of detailing, as discussed above, this proposed proportional adjustment approach will result in biased outcomes in terms of "excess" prescribing associated with Manufacturer Defendants.

82. In addition, under Dr. Rosenthal's model, it is impossible to distinguish between different allegedly wrongful detailing messages. In particular, contrary to what Dr. Rosenthal claims, she cannot adjust her model and thus revise her results if the fact finder finds that certain types of detailing messages were wrongful, but not all. Dr. Rosenthal's methods could not estimate "excess" prescription opioid MMEs in such an event.

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[133] "The Office of Prescription Drug Promotion (OPDP)," *U.S. Food and Drug Administration*, https://www.fda.gov/about-fda/center-drug-evaluation-and-research/office-prescription-drug-promotion-opdp, last accessed May 2019.

[134] Rosenthal Report, ¶ 75.

83. Dr. Rosenthal concedes that she did not use any data or statistical methods to separate the effects of detailing activities from non-detailing marketing activities,[135] or to identify which if any detailing messages were deceptive,[136] which physicians were exposed to them, where those physicians were,[137] and whether they relied on those allegedly deceptive detailing messages to write opioid prescriptions that would not otherwise have been written and were not medically appropriate.[138]

84. This is a critical oversight on Dr. Rosenthal's part. As I described above in Section V.A, a multitude of factors impact physicians' prescribing decisions, and many of these factors are more impactful than detailing. Thus, for each opioid prescription written by a physician, it is important to know the impact, if any, the allegedly wrongful information the physician received from the pharmaceutical manufacturer had on the prescribing physician's decision.

85. Dr. Rosenthal attempts to avoid these issues by stating that her methods are not trying to answer questions of "how marketing works", only "whether" marketing works in general.[139] However, fundamentally, assessing causal relationships requires something more rigorous than just understanding "whether" two sets of data "work" (or in statistical terms, correlate) with each other; it requires a fact specific inquiry into "how" those two data series might work together, utilizing a model formulation with properly constructed variables consistent with economic theory.[140] Dr. Rosenthal does not seem to address the right question, and this error impacts the statistical model she sets up as well.

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[135] Rosenthal Dep., 156:16–24 ("Q. What if the court finds that only journal advertising were unlawful? How would your model account for that? A. Well, as I believe I say in my report, the journal advertising data is very spotty for these drugs, so I've not included that as a separate factor. It's already out of my model. I would have to give that some consideration.").

[136] Rosenthal Dep., 147:14–23 ("What if the court concludes that any detail over five minutes in length were presumed unlawful, but anything shorter than that isn't? How can you quantify the impact of the over-five-minute visits in your model? A. As I sit here, I don't know because I haven't thought about it. Clearly I would need some data on the length of details."); Rosenthal Dep., 154:10–17 ("How would your model work if the court finds that only detailing visits where the representative spoke about addiction risk were unlawful? A. I don't know the answer to that question. I have not thought about how one could parse that out, so I don't know as I sit here.").

[137] Rosenthal Dep., 240:25–241:1 ("I cannot disaggregate by geography or by physician.")

[138] Rosenthal Dep., 240:25–241:1 ("I cannot disaggregate by geography or physician."); Rosenthal Dep., 150:14–23 ("Q. So in your model, you could have unlawful promotion that leads to medically necessary scripts still? A. I was asked to quantify the impact of the alleged unlawful promotion, not to examine that question about whether that prescription itself was medically unnecessary, so -- so it's something I haven't looked at and I don't believe it's related to my charge.").

[139] Rosenthal Dep., 84:4–13 ("A. I think, again, you misunderstand what the utility of the Datta and Dave analysis is. It is an analysis that is designed to dig into how marketing works and not whether. There would be no utility in comparing results of a Datta and Dave analysis, if one were possible, with my aggregate results because the questions they're looking at are entirely different.").

[140] Pearl, J. (2009), "Causal Inference in Statistics: An Overview," *Statistics Surveys*, 3, pp. 96–146, p. 99.

C. Dr. Rosenthal inappropriately uses an aggregate model, imposing the unrealistic assumption that all detailing has the same impact

86. Dr. Rosenthal sets up her model in the "aggregate" way, lumping all prescription opioid prescribing and all detailing together. However, assessing the right relationship, i.e., answering the "how" question instead of "whether" question, requires data that tracks prescribing decisions at the physician level. Academic literature, including that cited by Dr. Rosenthal, relies on this type of data to address questions related to pharmaceutical and healthcare markets.[141] The works cited by Dr. Rosenthal assert that "prescribing habits may be confounded by other unobserved physician-specific characteristics."[142] Dr. Rosenthal acknowledges that IQVIA, the company that provided the data she used for her analysis, "maintains a number of data streams that capture information on sales, promotion, and other statistics by individual drug over time."[143] Dr. Rosenthal chose to use two specific IQVIA data products that were at aggregate level, i.e., the National Prescription Audit ("NPA") and the Integrated Promotional Service ("IPS").[144] IQVIA NPA and IPS data are nationwide projections[145] and do not allow for the sort of analyses used in the above literature that relied on physician-level information. Based on my review of her report and analyses, Dr. Rosenthal does not acknowledge this type of physician-level data, let alone attempt to use it.

D. Dr. Rosenthal ignores that there is an endogenous relationship between detailing and prescribing

87. Dr. Rosenthal has not accounted for the fact that a firm's decisions on detailing and expected prescriptions are jointly determined. That is, firms incorporate their future expectation of sales into their decisions about detailing efforts, in terms of the frequency and breadth of information provided to physicians. This has long been recognized in the economic literature. There is no mechanism to account for this in Dr. Rosenthal's model. Failing to account for endogeneity in marketing can substantially upwardly bias estimates of the impact of promotion. Academic studies of the effects of marketing for pharmaceuticals

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[141] Datta, A. and Dave, D. (2016), "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics*, 26(4), pp. 450–468 ("Datta (2016)"), p. 452; Mizik (2004); Venkataraman (2007).

[142] Datta (2016), p. 455.

[143] Rosenthal Report, ¶ 51.

[144] Rosenthal Report, ¶ 51.

[145] "IMS MVP User's Guide," IMS, p. 3.

have found that accounting for this endogeneity substantially decreases the estimated impact of marketing on sales.[146] At least one study relied upon by Dr. Rosenthal has cited this endogeneity bias as a key concern, stating for example that, "physicians who already have a history of prescribing a particular drug or who have a higher unobserved likelihood of prescribing the drug (for instance due to their patient population or practice type) are more likely to be targeted by detailers."[147] Indeed, that work finds that detailing has an effect "substantially smaller than those in the literature based on aggregate information."[148] Dr. Rosenthal's results, therefore, likely overstate the impact of marketing due to her omission of this mechanism.

E. Dr. Rosenthal uses a negative depreciation rate that is inconsistent with marketing literature and the realities of the pharmaceutical industry

88. Dr. Rosenthal uses a *negative* depreciation rate of the impact of detailing visits which implies that a detailing message from many years ago has more impact on today's sales than does today's detailing. This use of negative depreciation rate is critical for Dr. Rosenthal's opinion about the relationship between detailing and "excess" prescribing. I describe these flaws in detail below.

89. In her econometric analysis, Dr. Rosenthal employs a parameter called a "depreciation rate" that is meant to capture the effect of past detailing that persists from month to month.[149] In plain language, what Dr. Rosenthal is trying to achieve by using this parameter is to assess the prolonged (or lagged) effect of detailing on physician prescribing decision. This concept is not controversial on its own, since marketing science has extensively studied the prolonged or lagged effects of advertising, or what it refers to as

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[146] As emphasized in the literature, advertising is jointly determined with price and quantity. As a consequence, most industry demand functions utilize simultaneous equation estimation methods to avoid ordinary least squares (OLS) estimation bias. *See, e.g.*, Berndt, E., Bui, L., Reiley, D., and Urban, G. (1995), "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *The American Economic Review*, 85(2), pp. 100–105. Similarly, my article on interindustry distribution of demand, which shows a decline in the advertising coefficient after correcting for endogeneity bias, was estimated using a 2 Stage Least Square method to prevent this bias. Grabowski, H. (1976), "The Effects of Advertising on the Interindustry Distribution of Demand," in *Explorations in Economic Research*, 3(1), pp. 21–75 ("Grabowski (1976)"), p. 29.

[147] Datta (2016), p. 452.

[148] Datta (2016), p. 450.

[149] Rosenthal Report, ¶¶ 33, 72.

"stock of goodwill."[150] What is controversial and flawed about Dr. Rosenthal's approach is what her model estimates the depreciation rate to be. Specifically, Dr. Rosenthal's model estimates a *negative* depreciation rate of -0.0067, which translates to an annual rate of -8.3 percent.[151] As Dr. Rosenthal herself admits, this "negative depreciation rate indicates that the stock of promotion grows over time."[152] The implication of this result is simple but crucial for Dr. Rosenthal's results: A detailing message from long ago has considerably more impact on today's sales than does today's detailing. For example, according to Dr. Rosenthal's model, prescription opioid sales in, for example, March 2009 are more strongly determined by detailing messages from 1997 than by detailing messages from March 2009. This is implausible and inconsistent with both standard business practices and academic research results.

90. Reliable models used in academic research to investigate the effects of marketing recognize that people forget marketing messages if they are not repeated over time.[153] This economic intuition is also consistent with what academic literature finds, i.e., detailing conducted long in the past has *less* impact on sales today than marketing conducted today. For example, one study of the antidepressant market, which focus on multiple antidepressant medications, finds a depreciation rate of 15 percent annually, corresponding to a monthly depreciation rate of approximately 1.34 percent, which is in contrast to Dr. Rosenthal's negative estimate.[154] In her academic work, Dr. Rosenthal herself has conducted marketing research on the impact of promotions across several classes of pharmaceutical products, and found that accounting for the effect of promotions two months in the past had no impact on the model results relative to controlling only for contemporaneous promotions.[155] In other academic work in which Dr. Rosenthal estimated depreciation rates, she also found positive

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[150] Nerlove, M., and Arrow, K. (1962), "Optimal Advertising Policy Under Dynamic Conditions," *Economica*, 29(114), pp. 129–142, pp. 131–132.

[151] Rosenthal Report, ¶ 72.

[152] Rosenthal Report, ¶ 72.

[153] *See,* Grabowski (1976), p. 29; Hirschey, M. (1982), "Intangible Capital Aspects of Advertising and R&D Expenditures," *The Journal of Industrial Economics,* 30(4), pp. 375–390, p. 375 ("Consumers tend to forget brands and continuous advertising is needed to maintain a given rate of sales. Thus, advertising expenditures can be viewed as a capital good that depreciates over time and needs maintenance and repair."); Heiman, A., et al. (2001), "Learning and Forgetting: Modeling Optimal Product Sampling Over Time," *Management Science*, 47(4), pp. 532–546, p. 532.

[154] Berndt (2002), p. 16.

[155] Rosenthal, M., et al. (2003), "Demand Effects of Recent Changes in Prescription Drug Promotion," *Frontiers in Health Policy Research*, D. Cutler and A. Garber eds. The MIT Press, pp. 1–26.

depreciation rates, not negative ones.[156] In fact, I am not aware of a *single instance* in the academic literature that finds a *negative* depreciation rate, even in academic literature that studies the effect of marketing on addictive substances, such as cigarettes and alcohol. Indeed, Dr. Rosenthal is also not aware of any such instance in the literature.[157]

91. I note that this is a significant and direct contradiction to Dr. Rosenthal's assertion that her finding of negative depreciation is "perfectly consistent with an addictive product like opioids."[158] Dr. Rosenthal does not cite to any academic marketing literature to support this point.[159] First, a depreciation rate is about how much of a message a physician hears, how much it affects his/her prescribing decisions in a given period, and how much of that effect is maintained over time in a dynamic environment characterized by new clinical data, new brand and generic entry, and other significant competitive events. The potential for addiction or dependence has little bearing on these dynamic factors that influence depreciation rates for pharmaceutical marketing. Second, studies of the effect of marketing on rates of use of addictive substances, such as cigarettes and alcohol, find positive depreciation rates. As an example, when another one of Plaintiffs' experts, Dr. Jonathan Gruber, investigated the impact of marketing on cigarette smoking, he only assumed large, positive depreciation rates.[160] One recent strand of work studied the relationship between television brand advertising and alcohol consumption among U.S. youth, and assumed a half-life of one month, which corresponds to a monthly depreciation rate of positive fifty percent.[161] Seminal articles studying the cigarette industry have estimated positive annual depreciation rates ranging from 27 percent to upwards of 45 percent.[162] More recent work

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[156] Donohue, J., et al (2004), "Effects of Pharmaceutical Promotion on Adherence to the Treatment Guidelines for Depression," *Medical Care*, 42(12), pp. 1176–1185.

[157] Rosenthal Dep., 259:25–260:6 ("Q. Okay. As you sit here right now, do you know of any literature, whether related to nonaddictive or addictive products, that has a negative depreciation rate? A. I cannot point to any other study, no.").

[158] Rosenthal Report, ¶ 72.

[159] Rosenthal Report, n.103. Dr. Rosenthal instead cites to another Plaintiff expert in order to assert that addicted patients may require and/or seek more opioids over time.

[160] Gruber, J. and Koszegi, B. (2001), "Is Addiction 'Rational'? Theory and Evidence," *The Quarterly Journal of Economics*, 116(4), pp. 1261–1303, p. 1291.

[161] Ross, C., et al. (2015), "The Relationship Between Population-Level Exposure to Alcohol Advertising on Television and Brand-Specific Consumption Among Underage Youth in the US," *Alcohol and Alcoholism*, 50(3), pp. 358–364, p. 362; Siegel, M., et al. (2016), "The Relationship Between Exposure to Brand-Specific Alcohol Advertising and Brand-Specific Consumption among Underage Drinkers—United States, 2011-2012," *The American Journal of Drug and Alcohol Abuse*, 42(1), pp. 4–14, p. 8.

[162] Peles, Y. (1971), "Rates of Amortization of Advertising Expenditures," *Journal of Political Economy*, 79(5), pp. 1032–1058, p. 1032; Schnabel, M. (1972), "An Oligopoly Model of the Cigarette Industry," *Southern Economic Journal*, 38(3), pp. 325–335, p. 329.

studying smokeless tobacco continues to find large positive depreciation rates, even finding that the stock of advertising for cigarettes vanishes entirely after a year; this corresponds to a monthly depreciation rate of over positive 20 percent and an annual depreciation rate of positive 100 percent.[163] All of this literature is at odds with Dr. Rosenthal's results.

92. Moreover, Dr. Rosenthal's finding of a negative depreciation rate drives a highly implausible finding: in her model, "excess" prescribing reached its peak while prescription opioid prescribing and Manufacturer Defendants' detailing was steeply declining. Dr. Rosenthal correctly observes that opioid prescription amounts started falling substantially beginning in approximately 2012.[164] Dr. Rosenthal also documents the substantial decreases in total detailing over this time period.[165] And yet Dr. Rosenthal finds that it is over the years 2012-2018 that the percent of MMEs attributable to challenged promotion reaches its maximum, and indeed her estimate continues to grow over time throughout 2012-2018.[166] Specifically, while overall detailing declined from approximately 55,000 visits/month in 2012 to approximately [redacted] visits/month in 2018, and while MMEs declined from 18 billion/month to under [redacted] in the same time period, Dr. Rosenthal's estimates of the fraction of MMEs attributable to challenged promotion rose from 55.7 percent in 2012 to [redacted] percent in 2018.[167] This is a nonsensical result, and is only possible because Dr. Rosenthal's estimated stock of contacts is growing exponentially over time, so that early detailing visits overwhelmingly contribute to estimated "excess" prescribing in later years, even as detailing efforts decline over time and concerns about opioid abuse and misuse are widely disseminated.

93. Furthermore, Dr. Rosenthal's negative depreciation rate ignores the fact that the pool of physicians available to prescribe pharmaceuticals is not static over time. Physicians retire as they age and new physicians enter the market. Figure 4 shows the total number of prescribers of schedule II opioids from 1997 – 2017. Every year during this period, new physicians[168] entered the pool. Thus, while a negative depreciation rate assumes that opioid prescribing in, for example, March 2009 are more strongly determined by detailing visits

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[163] Dave, D. and Saffer, H. (2013), "Demand for Smokeless Tobacco: Role of Advertising," *Journal of Health Economics*, 32(4), pp. 682–697, p. 694.

[164] Rosenthal Report, Figure 2.

[165] Rosenthal Report, Figure 4.

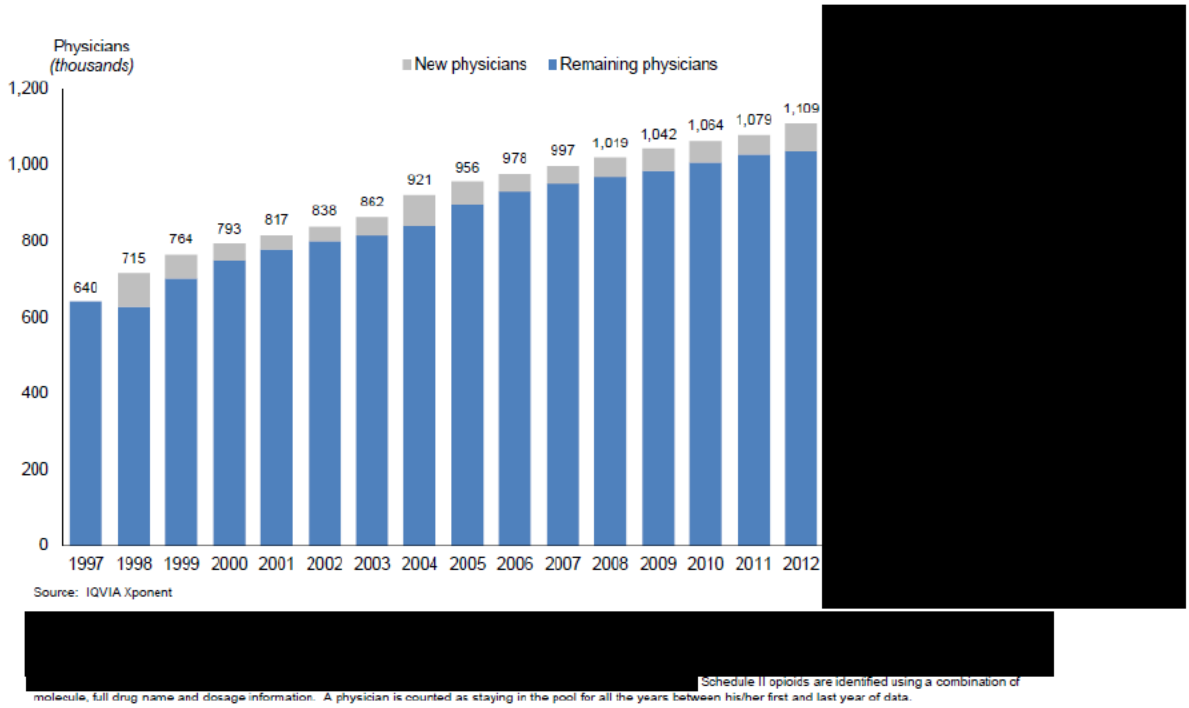
[166] Rosenthal Report, Table 2.

[167] Rosenthal Report, Table 2; Rosenthal Report Production.

[168] New physicians refer to both physicians who just started practicing and physicians who just started prescribing opioids.

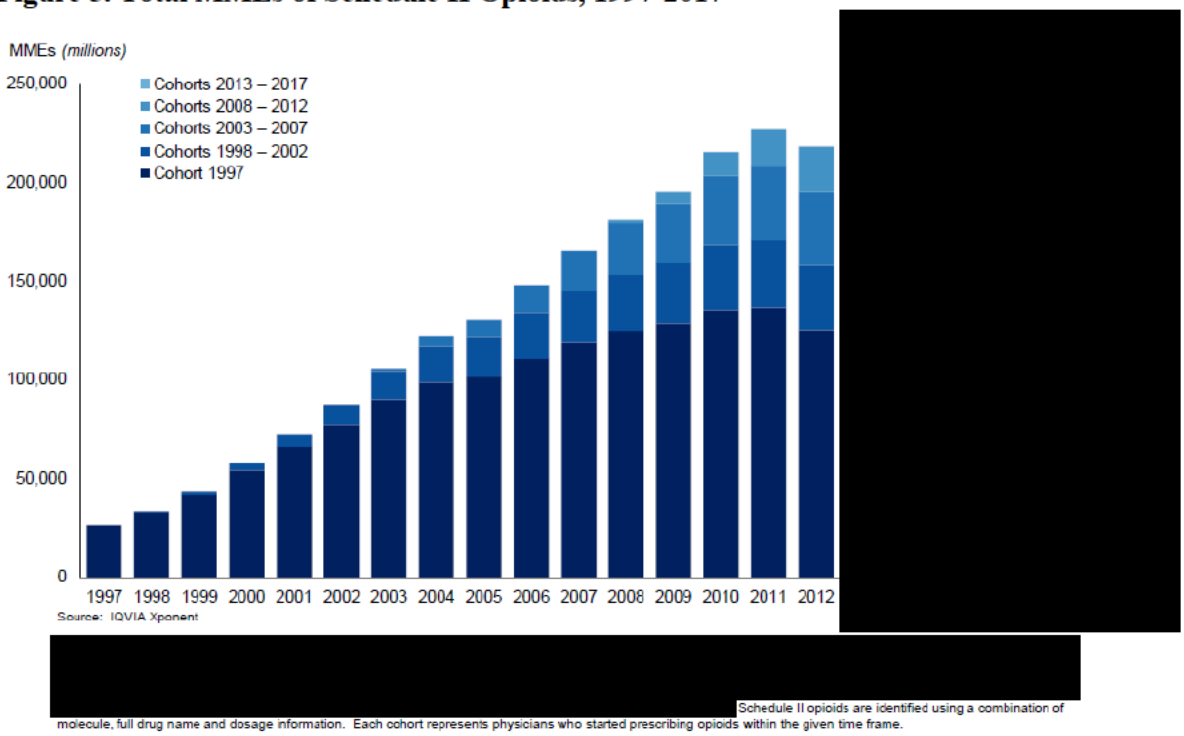
from 1997 than by detailing visits from February 2009, that assumption cannot be reconciled with the fact that many prescribing physicians in March 2009 were not even practicing in 1997, and hence could not have been subjected to the detailing visits from that time.

Figure 4. Total Schedule II Opioid Prescribers, 1997-2017



94. Moreover, if Dr. Rosenthal's theory of a negative depreciation rate were true, the percentage of total MMEs prescribed by earlier physician cohorts would have grown over time, due to the exponential impact of detailing visits in the early years. However, Figure 5 indicates exactly the opposite. The share of total MMEs prescribed by newer physicians grew significantly over time between 1997 and 2017.

Figure 5. Total MMEs of Schedule II Opioids, 1997-2017



F. Dr. Rosenthal identifies justifiable uses of opioids in her report, but does not account in her regression for the effect of marketing on prescribing for such uses

95. Dr. Rosenthal does not evaluate whether some or all of the detailing by Manufacturer Defendants was intended to promote prescription opioid medications for uses she considers justifiable. Nor does Dr. Rosenthal evaluate how her results would have changed if she had accounted for detailing of prescription opioids for appropriate uses.

96. In her report, Dr. Rosenthal claims to evaluate whether rising prescription opioid MMEs were intended to treat under-treated pain.[169] For this purpose, Dr. Rosenthal claims she "use[s] epidemiologic data and a simple simulation approach to approximate the portion of the increased prescribing caused by the allegedly unlawful promotion [that] could possibly be associated with using [prescription] opioids to address ostensibly 'under-treated' pain."[170] However, Dr. Rosenthal simply assumes that certain uses are appropriate and others are

[169] Rosenthal Report, ¶ 90.
[170] Rosenthal Report, ¶ 91.

not.[171] Dr. Rosenthal identifies the "justifiable uses" of prescription opioid medications as end-of-life cancer care, acute post-surgical care, and ER trauma incidents.[172] Thus, at best, as Dr. Rosenthal states, she calculates a "theoretical maximum"[173] on amounts of prescribing for these arbitrary "justifiable uses." She has not studied the link between these "justifiable use" prescription opioid MMEs and detailing, let alone studied the link between the "justifiable use" prescription opioid MMEs and allegedly *unlawful* detailing.

97. Indeed, accounting for the lawful detailing for uses that Dr. Rosenthal deems justifiable would change Dr. Rosenthal's but-for calculation significantly. Making no changes to Dr. Rosenthal's model other than assuming that detailing made to oncologists, surgeons, and anesthesiologists (i.e., physicians who specialize in conditions for which Dr. Rosenthal concedes prescription opioid medication use is "justifiable") is appropriate, there is a [redacted] percent reduction in the impact of alleged misconduct on MMEs.[174] Specifically, while Dr. Rosenthal finds [redacted] percent of the MMEs in 2018 to be "excess" MMEs,[175] just accounting for the foregoing appropriate use specialties reduces the "excess" MMEs to [redacted] percent under her model. This represents a [redacted] percent reduction. Results are similar for the remaining years for which Dr. Rosenthal calculates "excess" prescribing.[176] This is a considerable difference and indicates that Dr. Rosenthal's calculation is unreliable.

G. Dr. Rosenthal fails to include any reasonable control variables in her model

98. As discussed above, Dr. Rosenthal's preferred direct regression method aims to statistically explain the change in total MMEs in the U.S. by using only two factors: total detailing by prescription opioid manufacturers, and a prescription opioid price index she

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[171] Rosenthal Report, ¶ 92. Dr. Rosenthal assumes: "(i) that, at most, opioids are properly indicated for the short-term treatment of severe acute pain (e.g. trauma or post-surgical pain); end-of-life pain/hospice care; and cancer pain from active malignant disease; (ii) that chronic opioid therapy is not recommended for most common chronic pain conditions (defined as moderate to severe pain lasting beyond 60 to 90 days), including low back pain, centralized pain such as fibromyalgia, and headache pain; and (iii) that in less common chronic pain conditions (such as pain from advanced multiple sclerosis, sickle cell disease, pain following spinal cord injury and paraplegia, or post-herpetic neuralgia), which comprise a small percentage of chronic pain patients, opioids may be considered a third-line therapy (taken if other therapies are ineffective or contraindicated) for moderate and severe pain."

[172] Rosenthal Report, Appendix D, page D8.

[173] Rosenthal Report, ¶ 94.

[174] Excess prescription opioid shipments for this sensitivity are shown in comparison to those found by Dr. Rosenthal in Exhibit 2A and 2B.

[175] Rosenthal Report, Table 2.

[176] The minimum percent reduction is [redacted] in 2018 and the maximum percent reduction is 42.4 in 1997. *See* Exhibit 2A.

constructed. A robust statistical model should test her hypothesis that an explanatory variable (in this case detailing visits) helps explain the observed trend in prescription opioid MMEs. Specifically, a robust statistical model should explore whether there are other variables, called control variables, which explain some or all of the observed trends in prescription opioid prescribing. Failing to do so results in what is called "omitted variable bias," which in this context means that the effects of some other potential causes of the increase in prescription opioid MMEs, not accounted for in Dr. Rosenthal's model, are incorrectly ascribed to detailing.[177] In Dr. Rosenthal's case, this would mean that the fraction of prescription opioid MMEs that her model attributes to detailing may be artificially inflated.

99. For example, while Dr. Rosenthal considers variables representing the impact of important events in the relevant years, such as the introduction of JCAHO pain standards in 2001, her chosen model ultimately excludes the impact of those events.[178] Dr. Rosenthal's decision to ignore these types of events is incorrect because two of the events are statistically significant.[179] Dr. Rosenthal, ignoring that two of the events were individually statistically significant, incorrectly asserted in her opening report that the five events she considered were "[j]ointly…not statistically different from zero."[180] Dr. Rosenthal failed to observe that in typical cases, if control variables are individually significant, they must also be jointly significant.[181] In her errata, Dr. Rosenthal reverses this claim, stating that the individual events *are* jointly significant, but offers no further defense of why, if these important events are statistically significant, she has omitted them from her model.[182] Notably, Dr. Rosenthal finds that including these five control variables in her regression reduces her estimates of the impact of the stock of contacts, and yet she excluded them.[183]

100. Other important factors besides individual events are also of potential importance. As one example, Dr. Rosenthal's model does not consider whether some or all of the increase in

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[177] Wooldridge, J. (2009), "Multiple Regression Analysis: Estimation," in *Introductory Econometrics A Modern Approach*, South-Western Cengage Learning, p. 93–94 ("Wooldridge (2009)").

[178] Rosenthal Report, ¶¶ 73–74.

[179] Rosenthal Report, Table 1. However, Dr. Rosenthal finds a counterintuitively positive sign for the impact of Hydrocodone rescheduling in October 2014.

[180] Rosenthal Report, ¶ 73.

[181] Wooldridge (2009), p. 117. Indeed, Dr. Rosenthal cites a test of joint significance in her appendix and reports a p-value of .0176. Therefore, the five events are actually jointly significant at a 5% level, a conventional significance level, and are almost significant at 1% level. *See* Rosenthal Report, Table D.3.

[182] Rosenthal Report Errata, p. 2.

[183] Rosenthal Report, Table 1.

prescription opioid MMEs was due to an increase in total overall demand for healthcare. For example, from 1997 through 2016, the total number of prescriptions filled in the U.S. increased by 85 percent while inflation-adjusted per-capita spending on retail prescription medications increased by 159 percent.[184] As total overall demand for healthcare increases, one should expect demand for prescription opioid medications to increase concurrently; for example, there may be rising demand for prescription opioid medications as demand for surgeries increases. To account for this possibility, I augment Dr. Rosenthal's model with total healthcare expenditures over the relevant years, deflated by a medical CPI index.[185] I find that this proposed control variable has statistically significant predictive ability.[186] Failing to control for these additional predictors is a considerable oversight in Dr. Rosenthal's model and results.

H. Controlling for the above errors substantially impacts Dr. Rosenthal's results

101. Controlling for the above errors substantially impacts Dr. Rosenthal's results. Specifically, when I address just the issues I identified above, Dr. Rosenthal's estimates of "excess" MMEs are reduced substantially, ranging from being reduced by approximately 70 percent to being eliminated entirely.[187] These issues are:

a. Dr. Rosenthal's use of a negative depreciation rate is inconsistent with the realities of physician turnover and with the marketing literature's understanding of the impacts of detailing over time. I therefore consider positive depreciation

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[184] "Too Many Meds? America's Love Affair With Prescription Medication," *Consumer Reports*, August 3, 2017, https://www.consumerreports.org/prescription-drugs/too-many-meds-americas-love-affair-with-prescription-medication/, last accessed May 2019; "What are the recent and forecasted trends in prescription drug spending?," *Peterson-Kaiser Health System Tracker*, February 20, 2019, https://www.healthsystemtracker.org/chart-collection/recent-forecasted-trends-prescription-drug-spending/#item-start, last accessed May 2019.

[185] I construct this variable by first taking quarterly personal consumption expenditures on health care services from Federal Reserve Economic Data, dividing each quarterly observation evenly across the months of that quarter to arrive at monthly data, and deflating with a price index representing the consumer price of medical care for all urban consumers. *See* U.S. Bureau of Economic Analysis, Personal consumption expenditures: Services: Health care [DHLCRC1Q027SBEA], retrieved from FRED, Federal Reserve Bank of St. Louis; https://fred.stlouisfed.org/series/DHLCRC1Q027SBEA, April 29, 2019, last accessed May 2019; U.S. Bureau of Labor Statistics, Consumer Price Index for All Urban Consumers: Medical Care [CPIMEDSL], retrieved from FRED, Federal Reserve Bank of St. Louis; https://fred.stlouisfed.org/series/CPIMEDSL, April 29, 2019, last accessed May 2019.

[186] *See* Exhibit 1, demonstrating the statistical significance of this control variable across six sensitivities.

[187] *See* Exhibit 2. I note that Dr. Rosenthal's produced code contained an error in its calculation of but-for MMEs, preventing the produced code from recreating excess MMEs that match Dr. Rosenthal's Table 2. I have corrected the error by manually recreating the calculation of excess MMEs, but my results still do not match the version of Table 2 that appears in Dr. Rosenthal's report. I present two versions of my results in Exhibits 2A and 2B: One version obtains from using Dr. Rosenthal's code for calculating excess MMEs as produced, and the other obtains from my correction of Dr. Rosenthal's code for calculating excess MMEs. I arrive at the same conclusions from each.

rates, and in order to conduct a robust analysis I present results across a range of depreciation rates. I first consider an annual depreciation rate of 15 percent, consistent with the range of depreciation rates found in the marketing literature discussed above. I next consider an annual depreciation rate of 1 percent, to examine the degree to which Dr. Rosenthal's results hinge on a negative depreciation rate, instead of just one that is small. I lastly consider a depreciation rate of 99 percent monthly, in which the stock of contacts erodes almost entirely every month, and the variable of interest becomes approximately equal to detailing visits.[188]

b. I add total deflated healthcare expenditures as a control variable.[189]

c. I consider both a version of these sensitivities preserving Dr. Rosenthal's use of multiple breaks in the impact of detailing, and one in which (1) Dr. Rosenthal's unexplained 2002 break is removed, and (2) Dr. Rosenthal's unexplained August 2010 trend break in the impact of detailing is replaced by an independent time trend.[190]

d. I control for marketing for what Dr. Rosenthal acknowledges are justifiable uses of prescription opioid medications.[191]

102. The results of these adjustments, shown in Exhibit 2A and 2B, are evidence that Dr. Rosenthal's analysis is subject to numerous biases that overstate the impact of the alleged wrongful conduct, and fails to provide a reliable basis for analyzing the effects of the alleged wrongful conduct on prescribing.

I. Dr. Rosenthal does not establish a link between Endo's detailing of its prescription opioid medications and the sales (or shipments) of Endo's prescription opioid medications, and fails to put forth a methodology capable of reliably doing so

103. As I discussed above, Dr. Rosenthal devises a model in an attempt to identify the relationship between prescription opioid sales and prescription opioid detailing. She creates

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[188] *See supra* Section VII.E.

[189] *See supra* Section VII.G.

[190] *See supra* Section VII.C.2. In using an independent time trend, I set the beginning of the trend at the date in which total MMEs were at their maximum, which I find to be March 2011.

[191] As noted above in Section VII.F, this sensitivity alone eliminates approximately 40 percent of Dr. Rosenthal's estimated excess shipments. *See* Exhibit 2.

her model using national level data that aggregates prescription opioid shipments and prescription opioid detailing across all Defendant Manufacturers. Dr. Rosenthal uses her model to predict the "share of excess shipments," under the assumption that "all or virtually all promotion by the manufacturer Defendants from 1995 to the present was unlawful."[192] Since Dr. Rosenthal's model uses aggregate data, her estimates are also in the aggregate: for each year, she puts forth a single estimate of the share of excess total prescription opioid shipments, allegedly due to the total detailing of all of Defendant Manufacturers.[193]

104. When Dr. Rosenthal presents her estimates, she does not attempt to apportion the total share of excess shipments she calculated among the defendants, whether to Endo or anyone else. For example, Dr. Rosenthal claims that 5.5 percent of the MMEs in 1995 were due to "challenged promotion" from the defendants.[194] But she does not attempt to calculate what portion of that 5.5 percent was due to Endo's alleged misconduct, or what portion was due to alleged misconduct by any other defendant. Instead, Dr. Rosenthal proposes to perform additional calculations (that are not included in her report) to address these issues. Specifically, Dr. Rosenthal claims that she can "produce impact estimates for any combination of Defendants and years for which the plaintiffs can prove unlawful conduct," as well as other scenarios,[195] claiming that "[a]ny combination of these considerations can be accommodated with the analysis developed here."[196]

105. The key in Dr. Rosenthal's claim is the underlined part: this explanation, as well as a review of Dr. Rosenthal's work product and her examples in Table 3 and Appendix D of the Rosenthal Report, demonstrates that, to calculate share of excess shipments due to any one defendant, Dr. Rosenthal is proposing to use the same national, aggregate model she developed. The only difference would be that the model will be used to make predictions under different assumptions.

106. Throughout this report, I have established that Dr. Rosenthal's model suffers from numerous problems. Specifically, the model cannot be used to establish a causal link between detailing and prescription opioid shipments, and fails to create reliable estimates due to a myriad of conceptual and methodological errors. Dr. Rosenthal's proposal to use the

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[192] Rosenthal Report, ¶ 75.
[193] Rosenthal Report, Table 2.
[194] Rosenthal Report, Table 2.
[195] Rosenthal Report, ¶ 77.
[196] Rosenthal Report, Attachment D, p. D6 (emphasis added).

same model, just under different assumptions to investigate different scenarios does not cure the errors underlying the construction of the model in the first place.

107. No matter what assumption she uses, Dr. Rosenthal's model cannot establish a link between, for example, detailing by Endo and prescribing. Therefore, Dr. Rosenthal's model cannot generate reliable estimates of "excess" MMEs due to Endo's alleged misconduct.

108. Additionally, Dr. Rosenthal has identified zero detailing conducted by Par. Indeed, Par did not conduct any detailing for its prescription opioid medications, as supported by Dr. Rosenthal's own analysis of IQVIA data. Thus, Dr. Rosenthal's model cannot in any event reliably be used to show that detailing by Par (there was none) had an impact on prescribing.[197]

109. At the request of counsel, I have analyzed IQVIA data sets that contain market share information. On the basis of the information contained in those data sets, I quantified certain market share information, as set forth in Appendix 4.[198]

VIII. CONCLUSIONS

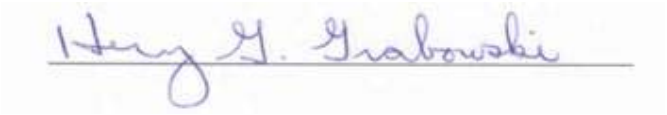
110. Dr. Rosenthal presents a limited and biased view of the pharmaceutical industry and, as a result, she attributes undue influence to manufacturers. Dr. Rosenthal fails to account for numerous other non-marketing related factors that impact physician prescribing decisions, and she also makes a series of flawed assumptions regarding marketing activities in the pharmaceutical industry, rendering the foundation of her statistical framework flawed and unreliable. Furthermore, Dr. Rosenthal's framework suffers from a series of conceptual mistakes. When I control for these conceptual mistakes, Dr. Rosenthal's estimates of "excess" MMEs are eliminated entirely, demonstrating the substantial biases present in her estimates of excess MMEs. Since Dr. Rosenthal's statistical framework is flawed and cannot be used reliably to address the relationship between pharmaceutical detailing and opioid prescribing, her methodology and conclusions she reaches relying on that methodology

[197] Dr. Rosenthal calculates "excess" shipments by first predicting MMEs from her regression using actual levels of detailing, and then predicting MMEs from her regression model setting allegedly unlawful detailing equal to zero. Dr. Rosenthal characterizes the difference in the two predictions as "excess" shipments. Because Par did not conduct any detailing, these two calculations yield identical MME predictions, and so Dr. Rosenthal's estimate of "excess" shipments would be zero.

[198] These data sets can be sorted in additional ways depending on the information sought, and I reserve the right to present additional information from this data at deposition or trial, including through demonstratives or other graphics.

cannot be used to show that detailing by pharmaceutical manufacturers led to "excess" MMEs.

Executed this 10th of May, 2019



Henry Grabowski, Ph.D.